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SYMPOSIUM ON TROPICAL MEDICINE*

INTRODUCTION

TROPICAL MEDICINE IN THE UNITED STATES AS A RESULT OF THE WAR

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In a broad sense tropical medicine is not a separate branch of medicine. Persons who have lived or visited in the Tropics at times come to the physician back at home with this dreadful appeal: "Doctor, I have a rare tropical disease. Can you cure me?" Actually there are very few diseases, such as African trypanosomiasis and yaws, which are peculiar to hot climates. Most diseases of tropical areas are also mildly endemic, or potentially endemic or epidemic in temperate zones, given only the necessary epidemiologic setting. Likewise, most of the diseases of temperate climates occur in the Tropics.

It is true, however, that warm climates produce an unusually satisfactory setting for the propagation of human disease, due to the following conditions:

(1) A greatly reduced threshold of resistance of human population to the development of etiologic agents of disease.

(2) Poor personal hygiene and group sanitation of native peoples.

(3) Unusually fine opportunities for the breeding of insects and other transmitters of disease agents, and

(4) The frequently enhanced virulence of the etiologic agents, especially for non-immune persons or groups entering hyperendemic areas.

Thus, tropical medicine may be properly considered as the science and practice of medicine in warm climates.

There is no need to discuss cosmopolitan diseases prevalent in warm climates, but it is desirable to consider some of the more common diseases of the Tropics which are less prevalent in our own country and their importance to us, now and in the years immediately ahead.

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THE DISTRIBUTION AND EPIDEMIOLOGY OF IMPORTANT TROPICAL DISEASES OF THE WAR AREAS

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The purpose of this presentation is to serve as an introduction to the discussions to follow regarding some important diseases existing in the present war areas that may be either introduced into, or increased in the United States as a result of military travel and commerce. The salient features of the epidemiology and geographical distribution of these diseases will be briefly reviewed.

The present active combat areas are in Europe, with ground operations in western Russia and in central Italy, and in the southwestern Pacific region, particularly New Guinea and the neighboring islands. Activity will extend into central Europe, into the vast tropical areas now occupied by Japan, including Burma, Thailand, French Indo-China, coastal China, the Ma-

lay States, the Netherland East Indies, the Philippine Islands, and into Japan itself. Troops in these areas will be exposed to diseases that are absent or of relatively low incidence in the United States. Equally important from this point of view are the widely scattered tropical and subtropical localities where American forces are now stationed outside the combat zones proper, hence the West Indies, Central America, the Galapagos Islands, British Guiana, Brazil, North and Central Africa, the Near East, India, free China, Australia, New Zealand, Fiji, Samoa, and Hawaii.

The main trade routes between North America and Europe (North Atlantic), Brazil and Africa (South Atlantic), through the Mediterranean and Red Sea, across and around Africa to India, and from the Pacific Coast of North America to Australia and the Pacific islands all afford opportunity for the rapid spread by ship or airplane of disease in returning troops or in arthropod vectors. Many diseases normally confined to, or particularly virulent in tropical areas may by these means be carried back to the United States as a result of the greatly increased traffic consequent upon the conduct of the war. It is, therefore, of interest to summarize briefly the cause, manner of dissemination, and circumstances favoring the occurrence or introduction of diseases potentially capable of assuming greater importance in the United States by importation from foreign endemic foci.

MALARIA

Malaria is caused by certain blood-inhabiting protozoa (*Plasmodium vivax, P. malariae, P. falciparum, and P. ovale*) which attack man only. It is normally transmitted through the bites of anopheline mosquitoes that have become infected by parasites ingested with an earlier blood meal.

Man possesses no absolute natural or acquired immunity, and no means of vaccination has been perfected. Recurrent attacks and relapses which may occur several years after infection make the victim a potential source of the disease for extended periods. Suppressive drugs (quinine, atabrine) hold the parasites in check only temporarily.

The dissemination of the disease requires the presence of the parasite in man, sufficient warmth, humidity and rainfall for the propagation and survival of the mosquito transmitters, and suitable water to serve as breeding places within flight range (one to five miles) so that sufficient anophelines are present to enable continued transmission. Natural breeding places may be augmented as a result of faulty agricultural or engineering practices that produce shallow standing water. Exposure to bites of infected mosquitoes is most likely to occur in poorly constructed or screenless houses, or outdoors after sundown. Failure to rid the blood of parasites as a result of inadequate treatment provides a source of infection for the mosquitoes and the community.

Though already endemic in the southern United States, the incidence and severity of malaria may be increased by the importation of more virulent strains of malaria parasites in man. More efficient mosquito vectors may also enter the country by ship or airplane and become established, if precautionary measures are not continually enforced.

Malaria is worldwide in distribution in the Tropical Zone and warmer parts of the Temperate Zones, with the heaviest foci in Central America, northern South America, northern and equatorial Africa, central U. S. S. R., coastal India, and the East Indies. The Pacific combat area is highly malarious and the disease is common in the Italian battle zone. Malaria is not indigenous and anopheline mosquitoes are said to be absent in the Pacific islands southeast of the New Hebrides, for example, in New Zealand, Guam, Tahiti, Samoa, Fiji, and Hawaii.

THE ENTERIC INFECTIONS

The important enteric infections include amebiasis, caused by the protozoön *Endamoeba histolytica*, bacillary dysentery, caused by *Shigella* spp., typhoid fever, caused by *Eberthella typhi*, and cholera, caused by *Vibrio comma*. All are human diseases transmitted through fecal contamination of food or water by human carriers,

by insects (flies, roaches, ants) which carry the microörganisms mechanically, or through faulty sewerage systems.

Man may perhaps have some natural or acquired resistance to amebiasis and bacillary dysentery, though immunity as a result of infection is questionable and there is at present no effective means of vaccination. Typhoid and cholera infections usually confer good immunity, and vaccination is effective.

These diseases originate from infected patients and their dissemination is favored by poor sanitation, faulty sewerage and water supply, inadequate inspection of food handlers, inadequate control and protection against flies and other insects (faulty garbage disposal, inadequate screening, exposure of food), and crowding in poorly sanitated quarters. The use of human feces as fertilizer for food crops may be an important source of infection. Warm weather is conducive to dissemination by favoring the propagation of insect carriers as well as the multiplication of bacteria causing the diseases.

The enteric infections are worldwide in distribution, except cholera which occurs mainly in India and the Orient and is not endemic in the United States. Although the other diseases are already present here, the possibility exists that more virulent strains of the pathogens may be introduced into the United States from the Tropics by the migration of infected human beings from endemic foci.

THE TYPHUS GROUP OF FEVERS

The rickettsioses (typhus and spotted fevers) are caused by rickettsia microörganisms transmitted by blood-sucking arthropods. Epidemic typhus caused by *Rickettsia prowazeki* var. *prowazeki*, is transmitted from man to man by human lice through contamination of skin abrasions or mucosa with fresh or dry louse feces or by crushing lice, and probably also by inhalation of dry rickettsias. Endemic or rat typhus, caused by *R. prowazeki* var. *mooseri*, is found in domestic rats and mice and is transmitted to man by rat fleas via infected flea feces. Spotted fever, caused by *R. rickettsi*, is transmitted by the bites of ticks, and Oriental mite typhus (*R. orientalis*) by the bites of larval mites (chiggers, *Trombicula* spp.).

There is no evidence of natural immunity to these infections, but acquired immunity follows infection or specific vaccination (partial in spotted fever).

Circumstances favoring infection are correlated with the habits of the vectors. Epidemic typhus occurs in louse-infested populations where unhygienic conditions exist as a result of poverty, crowding, war or famine, and is favored by cold weather conducive to increased lousiness. Rat typhus occurs sporadically through exposure to fleas in rat-infested dwellings or working quarters during warm weather. Spotted fever is contracted in warm weather through outdoor exposure to tick bites during occupation or recreation in rural or suburban locations, or from ticks carried indoors by dogs. Mite typhus likewise is contracted through outdoor exposure to chigger bites in endemic regions.

Rat typhus and spotted fever are endemic in the United States. Epidemic typhus is absent and lice are uncommon, but importation in human beings, lice, or perhaps dry louse feces in clothing is possible. Mite typhus does not occur here, and it is unknown whether our common chiggers could serve as vectors.

Louse-borne typhus occurs in Central and South America, Africa, Europe (especially in the Balkans and Russia), and Asia. Flea-borne typhus is present in all warm regions, spotted fever in North America, South America, Africa, and Europe, while mite typhus is confined to the Far East and Pacific area.

YELLOW FEVER

Yellow fever is caused by a filtrable virus which may be found in man and probably in wild forest animals in South America and Africa. The epidemic urban form of the disease is transmitted by the bites of the domestic yellow fever or "Stegomyia" mosquito, *Aedes aegypti*, and the endemic "jungle" form by various wild forest mosquitoes.

Man's natural resistance to infection is

probably variable, with permanent immunity following infection and for at least four years after vaccination.

The occurrence of the disease depends upon the presence of the virus in man or forest animals and the presence of susceptible mosquitoes to serve as transmitting agents. For urban epidemics, the yellow fever mosquito must be at least moderately common, breeding in or around 5 per cent or more of the dwellings. This is favored by the occurrence of standing water in undisturbed artificial receptacles about the home (flower pots, jars, cisterns, clogged roof-gutters, and the like) during the warmer seasons of the year. The yellow fever mosquito bites mainly during the day indoors, while other transmitters in the forest are outdoor daytime-biters, protection depending upon the use of proper screens, netting, repellents, or sprays. Unscreened patients may serve as infectors of mosquitoes during the early stages of the disease when the virus is circulating in the blood (from ten hours before to four days after the onset of symptoms).

While yellow fever is not endemic in the United States, the yellow fever mosquito is common in the South and could readily spread the virus if it were introduced in man or infected mosquitoes from endemic areas by fast transports, especially airplanes.

The disease is enzoötic, and in the past has been frequently epidemic, in tropical regions of South America and Africa. The yellow fever mosquito is distributed throughout the Tropics, including the Pacific and Indian areas where it constitutes a potential vector if the disease should be accidentally introduced in those regions.

Two other virus diseases, dengue and sandfly fever, deserve passing mention. The former is also transmitted by *Aedes aegypti* and related mosquitoes throughout the warmer parts of the world. The latter (also called Pappataci or Phlebotomus fever) is transmitted by sandflies of the genus *Phlebotomus* in areas extending from the Mediterranean region to South China. Sandflies of this kind are rare in the United States.

HEMOFLAGELLATE INFECTIONS

The hemoflagellate infections include the leishmaniases (kala azar, Oriental sore, and South American espundia), caused by protozoa of the genus *Leishmania*, and the trypanosomiases (African sleeping sickness and South American Chagas' disease), caused by protozoa of the genus *Trypanosoma*. These parasites are all found in man; those causing kala azar and Chagas' disease are also found in the dog, and the trypanosomes occur in domestic and wild animals in Africa and South America.

The leishmaniases are transmitted by sandflies (*Phlebotomus* spp.) through the bite or through crushing the insect on the skin, or sometimes by direct contact with the cutaneous lesions. African trypanosomias is transmitted by the bite of tsetse flies (*Glossina* spp.) and Chagas' disease by contamination of the skin or mucosa with the feces of infected blood-sucking triatomid bugs (family Triatomidae).

There is no evidence of natural immunity to these diseases, but in Oriental sore natural infection or vaccination confers immunity and in African trypanosomiasis arsenical drugs may afford some protection.

When the parasites are available, their dissemination depends upon an abundance of the insect vectors, which in turn requires favorable breeding conditions (damp débris, crevices, warmth and humidity for sandflies; shaded dry soil, brush, trees, game and domestic animals for tsetse flies; and poor building construction and rural living conditions for triatomid bugs). The tsetse flies are outdoor daytime biters, while sandflies and triatomids feed mainly at night, both in houses and outdoors. Warm weather increases the activity of insects and thus favors transmission of the diseases.

Hemoflagellate infections are not endemic in man in the United States, but the trypanosome causing Chagas' disease is present in rodents and triatomid bugs. Sandflies are rare and tsetse flies completely absent, and it is questionable that the diseases would become established here.

The two types of trypanosomiases are respectively limited to tropical Africa and to Latin America. The three types of leish-

maniases occur in Central America, South America, the Mediterranean region, Africa, India, and China.

FILARIASIS

Filariasis of different types is caused by several species of parasitic roundworms, the filaria worms, which are transmitted from man to man by mosquitoes and other blood-sucking flies. Bancroft's filariasis, caused by *Wuchereria bancrofti* and a related infection due to *W. malayi* are transmitted by the bites of mosquitoes, including domestic mosquitoes (*Culex* spp., *Aedes* spp.). Onchocerciasis, caused by *Onchocerca volvulus*, is transmitted by blackflies (*Simulium* spp.). Loaiasis, caused by *Loa loa*, is transmitted by deer flies (*Chrysops* spp.).

There is no natural or acquired immunity to these infections, no vaccination nor specific therapy is yet available, and the infections run a chronic course of many years' duration.

These diseases may be contracted wherever the parasites are present in the population and the specific insect transmitters are common as a result of suitable breeding places and warm weather favoring their propagation and activity. Infection involves exposure to mosquito bites in poorly screened quarters or outdoors, or to the bites of other vectors in their natural haunts near swamps or streams in endemic regions.

The diseases are not endemic in the United States, but suitable vectors are common and may constitute a potential hazard if the parasites are introduced by infected men returning from infected areas. Bancroft's filariasis is widespread throughout the Old World and New World Tropics, including all the Pacific islands except Hawaii. *Wuchereria malayi* occurs in India, China, and the Dutch East Indies. Onchocerciasis is endemic in equatorial Africa, Guatemala, and southern Mexico, and loaiasis in Central Africa.

SCHISTOSOMIASIS

Schistosomiasis is caused by three closely related species of parasitic worms, the blood flukes (*Schistosoma haematobium, S. mansoni,* and *S. japonicum*), which inhabit the blood vessels of man and, in the Orient, of domestic mammals and rodents. The eggs passed in feces or urine hatch in water, and the larval worms infect specific types of snails in which they multiply and develop into forms that later escape into the water and penetrate the skin of man during immersion.

Natural or acquired immunity is unknown, and infection depends upon exposure to "infected water" during wading, bathing, or washing.

These diseases occur where infected excreta are deposited in water, either directly or via sewage, in which there are susceptible snails. Their dissemination is favored by warm weather, agricultural practices like irrigation canals and rice cultivation, and living habits involving deposition of excreta in the water used for these purposes or for outdoor laundering, bathing, or religious ceremonies.

Schistosomiasis is not endemic in the United States, but it is possible that susceptible snails may be present. The disease is present in the West Indies and northern South America (*S. mansoni*), Africa (*S. mansoni, S. haematobium*), the Near and Middle East (*S. haematobium*), and the Far East, including the Philippines and Celebes (*S. japonicum*). The disease could be imported in infected human beings, and snail hosts may be introduced artificially or spread through irrigation projects.

With regard to other potentially important "tropical" diseases in the war areas, mention may be made of bubonic plague (transmitted by rat fleas), relapsing fever (louse- and tick-borne), yaws and bejel (transmitted by contact and probably by flies), and hookworm infection (contracted by contact with infested soil). With the exception of louse-borne relapsing fever, yaws and bejel, these are already endemic in the United States. As in the diseases discussed above, an increase of their incidence or severity here would depend largely upon conditions favorable for their transmission by arthropod carriers.

MALARIA

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That malaria will be introduced into the United States now and after the war by troops and other personnel, returning from highly endemic areas, is a foregone conclusion. At the same time, different and possibly more virulent strains of plasmodia may also be imported.[1] The effect of such a happening in a non-malarious area having suitable vectors may readily be imagined.

Of special importance to localities where anophelines are already prevalent are chronic relapsing cases as potential sources of infection to the local mosquitoes. While assuming that some species of mosquitoes are at present refractory to imported strains of malaria,[2] it is possible that long and repeated exposure to such strains may result in adaptation to them.

Furthermore, it would indeed be catastrophic if a mosquito species, similar to *Anopheles gambiae* transferred from Africa to Brazil in 1929,[3] should elude the sanitary precautions already in effect in this country.

These are only two of the broad problems of the post-war period in which it has been said that no place in the world will be more than 60 hours from the nearest airport. This prophecy has already been fulfilled.

This brings us to consider the individual patients who will be appearing in the offices of physicians throughout the country in ever increasing numbers. In addition to those who have symptoms, there is also the group of individuals who have been taking prophylactic quinine (or atabrine), which maintains symptoms at a subclinical level. The term suppressive medication is more desirable, for, when it is discontinued, there is the likelihood that a person with malaria will develop clinical manifestations.

Irrespective of the presenting symptoms, whether febrile or afebrile, persons, who have resided in areas where malaria is endemic or hyperendemic and are not well, are entitled to have suitable diagnostic examinations of their blood.

The severest forms of malaria have no resemblance whatever to the usual conception of the disease, as its manifestations can be most protean in character. I propose to mention briefly a few cases which illustrate this point, with special reference to those which had a fatal termination. It is indeed discouraging, in places where medical attention is available, that in this day and age men are continuing to die from malaria —a specific disease, for which there are specific remedies.

In order to emphasize the bizarre nature of the symptomatology I would like to refer to a number of cases, three of them in my own experience, in which other diseases are mimicked.

In Trinidad, a young adult oilfield worker and an elderly English lady were seen by the same physician within ten days. Both complained of attacks of pain in the gallbladder region and of fever in the afternoon. The physician had seen several such cases, and in spite of steadily rising temperatures, he persisted with only symptomatic treatment. In each case, vivax malaria was diagnosed by the daily thin blood smear.

In a well-equipped hospital, word was received to prepare the operating room for an "acute abdomen" (perforated gastric ulcer?), which was being sent in by special launch. The patient arrived packed in ice bags. He had a generally rigid abdomen with moderate temperature, a rapid pulse and a very anxious expression. Vivax malaria was demonstrated by a routine examination of the blood while a white blood count was being made, which resulted in his receiving intramuscular quinine rather than an exploratory laparotomy.

A ship's steward complained of mild diarrhea and abdominal cramps. Examination of the feces showed only an occasional red blood cell, leukocytes and epithelial cells. Three such examinations were made before the blood was examined. Under atabrine treatment the diarrhea disappeared and further symptoms of falciparum malaria did not develop.

An even more severe type of intestinal manifestation is shown in the report of the

German prisoner-of-war who was admitted to a hospital with a diagnosis of dysentery of two months' standing. A thin smear of his blood revealed no parasites on October sixth. No further examination of his blood is recorded but he died on October 11 of cerebral malaria.

At the beginning of a voyage requiring two or three months from Aden, at the southern end of the Red Sea, to Freetown, West Africa, the mate of a cargo ship sailing around Africa, sought medical aid for vague gastric symptoms in five ports-of-call, and received prescriptions for alkalies. In one port, the physician made a careful physical examination and advised the removal of practically all of his teeth which were carious. In desperation the patient had all of his teeth removed and subsisted on liquid and soft diet for the rest of the journey. Arriving at Freetown he encountered a malaria-conscious physician, quartan malaria was diagnosed and treated, and improvement in his condition was apparent within five days.

Details have recently been recorded of eight cases of malaria in persons returning to this country within the past year from such tropical areas as cited above.[4]

A welder, returning to the United States from East Africa, waited for transportation in Accra, on the Gold Coast for about one week. He had a chill on arrival in Miami by plane on August 29. Three days later he consulted a physician for upper respiratory symptoms and was admitted to a hospital on the following day in a deep stupor; the temperature was 104° F., with approximately 50 per cent of the red blood cells showing *P. falciparum*. Treatment was started but he died of cerebral malaria eight days after landing in this country.

Another welder en route from Africa by plane also stopped for several days in Accra, reaching this country on February 4. On February 8, he had a routine clinical examination with no abnormal findings. There was no examination made of the blood. (Indeed it is doubtful if parasites could have been demonstrated in his blood as he was in the incubation period.) On February 15, he had chills, generalized aching, headache, nausea and vomiting, profuse perspiration and a temperature of 100° F., which resulted in a provisional diagnosis of grippe. The patient seemed to improve the following two days, then suddenly became worse. He was admitted to the hospital on February 18 with a temperature of 104° F., leukocytes 3,400, with no malaria parasites in the thin blood smear. On February 19 the patient became delirious, the temperature was 104° F., and he went into coma. Parasites were then found but it was too late for the intravenous quinine treatment administered and the patient died on February 21. The six other cases in this series with more fortunate results showed one or more of the following symptoms: fever, chills, pain in the chest, upper respiratory symptoms, labial herpes, vomiting and diarrhea and blackwater fever. In one instance the diagnosis was suggested by the patient himself.

Since the above cited cases all give a history of having been in the Tropics, one might be very prone to say, "Well, it can't happen here," but the following case never left the confines of the United States. A patient was admitted to a hospital on September 21, disoriented, irrational, and deeply jaundiced. The history was that his illness had been provisionally diagnosed as influenza on September 12, with a temperature of 104.8° F. He was admitted to a hospital on September 18 for three days, during which time the temperature was never over 100° F., the leukocytes were 7,000; a differential count was made without mention of parasites being found. Extensive blood chemistry was carried out on September 21, but again no mention is made of a search for parasites. The following day he went into coma and died. In the postmortem blood approximately one in every 10 red blood cells was found to be parasitized—falciparum malaria.

Falciparum or estivo-autumnal malaria is by far the most important as it can frequently be fatal, whereas vivax or benign tertian malaria is prone to relapse and quartan malaria may become chronic.

The suggestion has been made regarding the issuing of a card of instructions to passengers and crew members of all aircraft returning from the Tropics in which they are warned to obtain blood examinations for malaria at the onset of any symptoms.

The broad problem remains an epidemiologic one.

DIAGNOSIS

The diagnosis is made by demonstrating the parasite in the blood, which is most readily done by means of the thick film, a practice which should, ideally, be routine. If malaria is actually suspected and the first examination is negative, it should be repeated at intervals of twelve hours for a period of three days.

For those not familiar with the diagnosis, I should like to recommend a most useful and valuable manual which is available, from the Superintendent of Documents, Washington, D. C., (price, 30 cents.) It is Bulletin No. 180 of the National Institute of Health—"Manual for the Microscopic Diagnosis of Malaria." It has numerous plates showing the appearance of parasites in both thin blood smears and thick blood films.

The edition available hitherto does not contain directions for Field's rapid staining methods which is here briefly summarized and is soon to be demonstrated. For those who have experience with thick film preparations this stain is recommended as a rapid, efficient and simple office procedure which may be carried out while the history and temperature are being taken.

Preparation of Field's Stain.

Disodium hydrogen phosphate crystals (if anhydrous 10.0)	25.0 gm
Potassium dihydrogen phosphate	12.5 gm
Distilled water	1,000 ml.
For "Solution A" add to 500 ml. of the above	
Medicinal methylene blue Azure 1	0.8 gm
Azure 1 (Azure B)	0.5 gm
For "Solution B" to the remaining 500 ml. add	
Eosin, yellowish, water soluble	1.0 gm

To stain:

Allow rather thin thick films made with three or four small drops of blood to dry until drop no longer shines (drying may be hastened by gentle heating)
Dip 1-2 seconds in Solution A
Wash in distilled water or rain water
Dip 1-2 seconds in Solution B
Wash as above, drain, dry thoroughly and examine.

For those who have had little or no practice in the recognition of malaria parasites in thick blood films, a somewhat slower method of staining is the one of choice.* It is briefly, as follows:

Prepare even thick blood films
Allow to dry flat until no longer shiny
Dip for one second in dilute methylene blue solution
Wash gently in distilled water or rain water
Stain face down 5-10 min. in solution of Giemsa stain prepared by adding one drop of stain to 1 c.c. of buffered water.
Wash, drain, dry thoroughly and examine.

SUMMARY

1. That malaria will be introduced into the United States as a result of the war is already a foregone conclusion.

2. A number of case histories of malaria with bizarre manifestations are briefly mentioned.

3. A warning to physicians of the gravity of falciparum infections is given.

4. A rapid method for the staining of thick blood films is given and a further method for general use is recommended.

REFERENCES

1. Boyd, M. F., Stratman-Thomas, W. K., and Kitchen, S. F.: Technique for the use of malaria in paresis, Am. J. Trop. Med., 16: 324, 1936.

2. Boyd, M. F., and Kitchen, S. F.: Comparative susceptibility of malaria parasites, *ibid.*, 16: 70, 1936.

3. Soper, F. L., and Wilson, D. B.: *Anopheles gambiae* in Brazil 1930 to 1940., Rockefeller Foundation, N. Y. C., 1943.

4. Most, H., and Meleney, H. E.: Falciparum malaria: the importance of early diagnosis and adequate treatment, J. A. M. A., 124:71, 1944.

5. Field, J. W.: Further note on a method of staining malarial parasites in thick blood films, Trans. Roy. Soc. Trop. Med. & Hyg., 35; 35, 1941.

*A supply of the necessary materials for this method will be made available at cost to all members of the Orleans Parish Medical Society who apply to Mr. A. J. Kuhlman at the office of the Secretary of the Society. Directions for use and a specimen stained slide or normal blood will be included with the staining materials.

THE DYSENTERIES

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INTRODUCTION

The statement so frequently heard today that the present diseases of Africa and of the islands of the Pacific will be the future diseases of the remotest villages of America is exaggerated, as all generalizations tend to be. It is nonetheless based on literal truth. It is not inconceivable that within the next few years every physician will begin his investigation on every new patient with an inquiry as to whether he—or she—served in the armed forces of the United States, and if so, where. For today Americans from all parts of the country have gone to the four corners of the earth, and the diseases which they may contract there and which they may bring home with them concern the whole medical profession, particularly those of us whose primary interest is tropical medicine.

The possible introduction into this country of diseases which produce dysentery has an individual as well as an epidemiologic aspect. From the individual standpoint, the question immediately arises as to whether or not a person who is suffering from, or who has ever suffered from dysentery is likely to suffer in the future as the result of his disease. The answer naturally depends in part upon how promptly the condition has been diagnosed and how adequately it has been treated. Yet even when these criteria are met, the chances are that the person who has once had one or another of a certain group of dysenteric diseases may be affected by their sequelae, in some instances to the point of complete invalidism. This is true for two reasons: (1) Some of the acute dysenteries are characterized by a strong tendency towards recurrence; (2) dysentery never develops until some degree of intestinal ulceration has occurred. Intestinal ulceration of any degree is necessarily followed by scarring of some degree, which leads, at least in some instances, to recurrent or even permanent disability.

From the epidemiologic standpoint, the questions of the importation of the more common dysenteries as the result of the war is in one sense not important. The dysenteric diseases which soldiers are most likely to contract, and which therefore are most likely to be imported, are already prevalent in this country, and in no small numbers, at that. We are a supposedly hygienic nation. We have a vast store of information on, and we have applied our knowledge of, such subjects as sewage disposal, water purification, pasteurization of milk, insect control, and the non-use of human feces for fertilization. Yet in spite of this knowledge we have not yet eliminated the two most common dysenteric diseases, bacillary dysentery and amebic dysentery, which are the diseases soldiers are most likely to contract and to import.

It is not true, however, to say that the introduction of these diseases is of no importance at all. The types which are prevalent in the Tropics are possibly more virulent than those now prevalent in this country, and it is reasonable to postulate that the introduction of even a small number of cases of virulent dysentery might mean, in time, the dissemination through the country of the same virulent types. How to prevent this catastrophe is not, of course, the subject of this paper, which is concerned only with the possibility or the probability of their importation.

GENERAL CONSIDERATIONS

Before proceeding to a discussion of special varieties of dysentery, certain general considerations should be mentioned. One of them is the matter of nomenclature. Dysentery is a term which is rather generally misused. In the first place, and contrary to ordinary usage, dysentery is really the symptom of a disease and not a disease in itself. In the second place, and again contrary to ordinary usage, dysentery and diarrhea are not synonymous terms, and it is unfortunate that they are so often used as if they were. Some writers prefer to discard the term dysentery altogether and to describe all liquid stools as diarrheic,

differentiating them on the basis of whether or not they contain blood, but it seems more reasonable to retain both terms and to use them in their proper significance.

Diarrheic and dysenteric stools are similar in that both are abnormally frequent, both are unformed, and both contain mucus, but there the resemblances end. A dysenteric stool contains pus and blood in large amounts, while a diarrheic stool contains blood infrequently and pus even more infrequently. The chief distinction between them, however, is that a diarrheic stool is composed chiefly of fecal matter, very little of which appears in the dysenteric stool, whereas the dysenteric stool, as the result of intestinal ulceration, contains cellular débris, which is always lacking in the diarrheic stool, because intestinal ulceration is not a feature of diarrheic diseases.

In contrast to the numerous diseases in which diarrhea may be a symptom, the diseases which produce dysentery are limited, even in the Tropics, where they are more frequent than anywhere else in the world. Their incidence varies according to the country under discussion, but in general the four most common dysenteric diseases are bacillary dysentery, amebic dysentery, balantidial dysentery, and schistosomal (bilharzial) dysentery.

Of less importance, because they are not infectious, or because their incidence in this country is already high, or because they are not usually associated with dysentery, are lymphopathia venereum (lymphogranuloma inguinale), non-specific ulcerative colitis, salmonellosis, and brucellosis. In four other diseases, malaria, leishmaniasis (kala azar), carcinoma of the intestines, and tuberculosis, dysentery is observed only in the late or terminal stages. *Isospora hominis, Giardia lamblia, Trichomonas hominis,* and *Chilomastix mesnili,* although mentioned by a few authorities as responsible for dysenteric manifestations, either do not invade the intestinal mucosa or do not remain in the wall for a sufficiently long period to cause pathologic changes. In my own opinion the possibility of dysenteries of such origins is remote.

Although cholera produces diarrheic rather than dysenteric symptoms, it should at least be mentioned in a discussion of the dysenteries because it is a serious epidemiologic problem in the Tropics. The chances of its importation into this country are not great, since all soldiers in cholera areas have been vaccinated against it, and vaccination is generally effective, as are quarantine regulations. The vibrio is not usually carried by humans for very long periods of time, and its importation depends upon only three possibilities: (1) That mild infections might develop in vaccinated subjects; (2) that vaccinated subjects, while themselves not presenting clinical diseases, might become carriers of the organism; (3) that the disease might be brought in by persons ill with it, or persons in the incubation period, who are travelling by air.

Schistosomiasis, leishmaniasis (kala-azar), and malaria will be discussed elsewhere in this symposium and will therefore be mentioned only incidentally or disregarded completely in this paper.

BACILLARY DYSENTERY

The distribution of *Shigella,* the etiologic agent of bacillary dysentery, is world-wide, although species and types vary greatly in virulence in different parts of the world. The most virulent type now known, *Shigella dysenteriae* (Shiga), already exists in Japan and other parts of the Far East, and is likely to spread extensively by the exigencies of war. It is therefore reasonable to assume that as conquered territories are reconquered by our armies, outbreaks of these virulent types of dysentery will occur and will increase as the conquering armies draw closer and closer to the home islands of Japan.

Other problems must be faced in addition to those inherent in the acute disease. If certain observations in this field can be accepted, a small proportion of all patients with bacillary dysentery in later life develop non-specific ulcerative colitis, and the incidence of this disease may therefore be higher in the near future than we ever conceived that it could be, as a result of the presently increased incidence of acute bacil-

lary dysentery in the armed forces. This, however, will be a matter affecting only the individual victim and not one of importance from the standpoint of dissemination.

True explosive outbreaks of *Shigella* infection are relatively rare in general population groups. These organisms, however, frequently spread widely, although slowly, through such groups when they are introduced, and high prevalence ratios are commonly encountered. The chances of spread are particularly great whenever sanitary conditions are poor or overcrowding of the population is present.

Because bacillary dysentery is of both individual and epidemiologic significance, the therapy of the disease warrants brief mention, even in a paper of these limits. The introduction of sulfaguanidine and of succinyl sulfathiazole has not solved the problem, as once seemed likely. Both drugs relieve symptoms, it is true, and both cause *Shigella* to disappear from the stools, but neither of these immediate results in an adequate long term criterion of cure, from the standpoint of recurrence of the infection, reinfection, or the prevention of sequelae. My own experience makes me question the effectiveness of these drugs in chronic bacillary dysentery, in which, on the basis of clinical improvement and sigmoidoscopic evidence of improvement in the lesions of the intestinal mucosa, I secured good results in only three of 40 cases. It is interesting to observe that recent reports concerning them are considerably more guarded than were earlier reports.

On the basis, again, of the immediate criteria previously mentioned, sulfadiazine seems considerably more promising than either sulfaguanidine or succinyl sulfathiazole. Recent data indicate that it causes *Shigella* to disappear from the stools more rapidly than either drug, and that, using the criteria of symptomatic improvement and improvement in the state of the bowel wall, it is also more effective in the chronic type of bacillary dysentery. Unfortunately, sulfadiazine must be administered cautiously in the Tropics, where it would have its widest field of usefulness, because of the risk of kidney complications, which is enhanced as the result of the dehydration almost inevitable in warm climates.

AMEBIC DYSENTERY

The intestinal protoza *Endamoeba histolytica*, like the *Shigella* group, is of worldwide distribution. Wherever it is looked for it is found. In temperate climates the incidence of amebic dysentery is not high, the disease in these regions commonly occurring in the form of amebiasis. In the Tropics amebiasis is very common and is frequently the chief disease with dysenteric manifestations. Three factors are probably responsible: the low level of sanitation, the generally poor nutrition of the population, and unknown climatic factors.

The inability of *Endamoeba histolytica* to multiply, which reduces its epidemic potentialities, has already been mentioned. From the standpoint of the individual, however, amebic dysentery presents more serious problems than does bacillary dysentery. Spontaneous cures, with permanent disappearance of the parasite, occur in the great majority of all cases of bacillary dysentery, whereas in amebic dysentery no such immunity develops and the organism continues to inhabit the intestinal tract. The host thus becomes a cyst-passer and presents what is called asymptomatic amebiasis. Actually, the disease is frequently not asymptomatic, for after therapy the patient often realizes that symptoms were present of which he was not cognizant until he was rid of them.

Still another possibility must be considered. My own experience is that when patients with so-called asymptomatic amebiasis lost their resistance, as the result of such factors as exposure, overwork and exhaustion, they are prone to develop acute amebic dysentery. The acute phase of the disease may lead, in turn, to such complications and sequelae as amebic hepatitis, amebic liver abscess, perforation of the intestine, ameboma, amebiasis cutis, amebic abscesses of the brain, lungs or kidneys, and possibly, in later life, carcinoma of the intestine.

For these various reasons the therapy of

amebic dysentery and of amebiasis, like the therapy of bacillary dysentery, warrants brief mention. All patients who harbor the parasite, whether or not they present symptoms, should be treated. Emetine hydrochloride is probably more widely used than any other amebicide, and the general opinion is that it is a highly effective drug. The introduction of more refined methods of diagnosis, and particularly of the zinc sulphate technic, has thrown considerable doubt upon this belief. It is true that the drug is highly effective in relieving the acute symptoms of amebic dysentery, that it is the only drug effective in the therapy of ameboma (amebic granuloma) and in the various extra-intestinal amebiases just enumerated. But its curative effectiveness is probably less than 50 per cent in the dysenteric variety of amebiasis and less than 30 per cent in the non-dysenteric variety.

My own opinion, based on a personal experience of 126 cases of amebiasis treated with diodoquin, including 20 cases with dysenteric manifestations, is that this is the drug of choice in this disease. It was effective in 99 per cent of patients in this series, 92 per cent of whom were cured by a single course of treatment.

In connection with amebiasis, a personal observation might be mentioned, since, so far as I know, it has not been emphasized by any other worker in this field. It is that in a large percentage of cases symptoms persist for a time even after the infection is cured. Because this fact is not generally comprehended, cases such as the following can occur:

Early in 1941 a patient was referred to me from the central part of the United States, with a diagnosis of refractive amebiasis. She had contracted the disease in the Chicago epidemic of 1933, and trophozoites of *Endamoeba histolytica* had been found in her stools at the time. Dysenteric symptoms recurred after the first course of treatment, and a second course of therapy was at once instituted. The cycle of symptoms and treatment continued over the intervening seven-year period until some eighty full courses of therapy, including every known amebicide had been administered. Inquiry revealed that only the single stool examination had been made, immediately after the infection had been contracted, in 1933. Repeated stool examinations in 1941 were negative, as might have been expected: The concentrated therapeutic regimen had destroyed all the organisms, probably many years ago, and my only wonder is that it did not also destroy the patient, who was found to have brucellosis, which readily explained the persistence of the dysenteric stools.

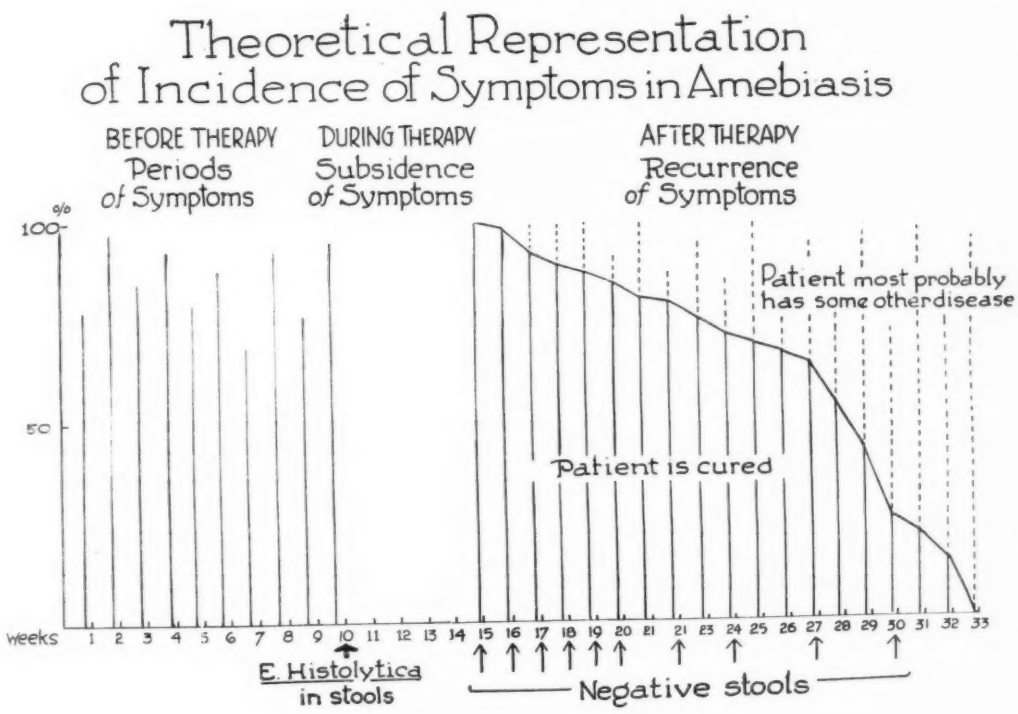
A diagram (p. 105) may clarify my point. A particular symptom, diarrhea (though any other symptom could be similarly presented), is depicted as occurring in weekly attacks for 10 weeks, in the form of eight to 10 diarrheic stools daily. Within two or three days after the institution of amebicidal therapy symptoms disappear, and they remain absent as long as therapy is continued. This practically always occurs, regardless of whether the amebicide is an organic compound, an iodine preparation, or an arsenical.

When therapy is discontinued, symptoms apparently due to amebiasis are likely to reappear after varying periods of time, and repeated attacks of diarrhea may again occur, though they diminish in severity with each recurrence. Regardless of the recurrent symptoms, amebicidal therapy should not be re-instituted unless and until organisms are again found in the stools, which should be examined at routine intervals as well as during exacerbations.

The physician who is not familiar with the sequence of events just outlined, and particularly with the tendency of symptoms to recur, though with diminished severity, for some time after parasites disappear from the stools, is likely to re-institute amebicidal therapy with each attack. As a result, as in the case described, the patient is likely to be treated beyond his needs for amebiasis, and whatever associated condition he may have is likely to be neglected.

BALANTIDIAL DYSENTERY

The parasite of balantidial dysentery, *Balantidium coli*, is a common intestinal



ciliate of the pig and the monkey and is world-wide in its distribution, though it is rare in man except in certain tropical countries. It is classified as a pathogenic parasite, and usually, when it penetrates the intestinal mucosa, the lesions and the resultant symptoms produce the general picture of amebic dysentery. It may, however, live in the human bowel without producing definite symptoms, though cysts are passed in the stools, and it may penetrate the mucosa without causing necrosis and ulceration. Although spontaneous cure occasionally occurs, cure by specific therapy is not readily achieved, and the disease may prove fatal in debilitated subjects, which makes it of individual importance.

Since the incidence of *Balantidium coli* is so high in hogs in America, while at the same time it is so low in human subjects, some factor as yet unknown probably plays a part in the possibility of individual infection. Until this factor is understood, it is impossible to say whether the introduction of a few cyst-carriers into the country is likely to cause any special problems after the war.

THE LESS COMMON DYSENTERIES

Lymphopathia Venereum (*Lymphogranuloma Inguinale*): Whether or not this disease is likely to be imported into the United States after the war can best be discussed by those concerned with venereal disease control, a part of which problem it is. General statements are difficult to make, since the infection has been recognized only in recent years. It is therefore scarcely fair to say that the increasingly large number of cases now being diagnosed represent a true increase in incidence.

Two complications of lymphogranuloma inguinale, ulcerative colitis and rectal stricture, may give rise to typically dysenteric stools, which may persist for months or years. At the present time these complications are infrequent. In the last two years, however, I have myself seen three or four times as many rectal strictures of this origin

as I saw in the preceding six years, a fact which I regard as significant, though I have no explanation for it. Lymphogranuloma inguinale also seems to be an increasingly frequent cause of nonspecific ulcerative colitis, though again the statement must be made with reservations: It is quite possible that it was an equally frequent unrecognized cause in the past.

For the present, lymphogranuloma inguinale is of importance to the individual rather than to the general population. A large increase in its incidence would be necessary to make it otherwise. On the other hand, it is fair to say that if the disease becomes more frequent, there will undoubtedly be an increase in both ulcerative colitis and rectal stricture as a result, and an increase, in turn, in dysentery of this origin.

Nonspecific Ulcerative Colitis: Although all dysenteries actually are forms of ulcerative colitis, since dysentery does not exist without intestinal ulceration, the term nonspecific ulcerative colitis is reserved for those types the etiology of which is unrecognized. The incidence of the disease obviously depends upon the diagnostic ability of the profession: The poorer the diagnosis from the standpoint of etiology, the higher will be the incidence. As just pointed out, recent increases in our knowledge of lymphogranuloma inguinale have removed a certain number of cases from this classification, and if the theory can be accepted that 80 or 90 per cent of the cases previously regarded as nonspecific ulcerative colitis are really instances of food allergy, some of the remaining cases in the group would also be removed.

Ulcerative colitis is of both individual and general importance. If diagnostic methods have failed and appropriate treatment is not applied, the prognosis for the individual is correspondingly poor. From the epidemiologic standpoint it may be postulated that some individuals with this disease are likely to harbor virulent strains of parasites, and that the longer their disease remains undiagnosed and untreated, the greater is the probability of its dissemination.

Salmonella Dysentery: All of the commonly described varieties of *Salmonella* have been found in this country, and in relatively the same proportions as in other areas of the world. Only a few special studies, however, have been carried out on dysenteric disorders caused by this infection. Some observers have reported cases of dysentery due to these organisms in the Tropics as well as in other areas. The incidence in the New Orleans area, according to James Watt (personal communication), who is now studying the problem, seems unusually high for the United States.

Although it is of course possible that certain strains of *Salmonella* tend to produce the dysenteric syndrome more frequently than others, there is no real evidence to confirm such a supposition. Since, therefore, all common types of *Salmonella* are found in the United States at present, the likelihood of importation of more virulent (dysenterogenic) strains is extremely remote.

Brucellosis Dysentery: Since Brucella infection is transmitted by infected cattle, and only occasionally, if at all, by man, brucellosis is not an epidemiologic problem, though it may show an increased incidence after the war, as the result of the careless and unauthorized drinking of infected milk by soldiers. The incidence of the disease is high in tropical countries, particularly the variety due to *Brucella melitensis*, though a dysenteric phase is unusual. In fact, one experienced observer, Mr. Ruiz Castañeda (personal communication), over a long period of time, saw only one case with dysenteric manifestations.

Our knowledge of brucellosis in this country is still not accurate, but the *abortus* variety is unquestionably the most frequent. In the last five years I have personally observed nine cases of *Brucella abortus* infection with dysenteric symptoms, in addition to the case already described in this paper as treated for amebiasis. Two other cases were also diagnosed as amebiasis, two as chronic bacillary dysentery, and the remaining five as nonspecific ulcerative colitis.

In all 10 cases diagnosis was made by consistently high agglutinations, especially during exacerbations, by positive skin tests, or by a positive opsonocytophagic index; at least two of these tests were positive in every case. All 10 patients improved symptomatically on vaccine therapy.

Unusual (Terminal) Dysenteries: Thrombosis of the capillaries of the colon occurs frequently in falciparum malaria, and diarrhea is a not infrequent complication of the disease, but secondary infection of the thrombosed areas is unusual, ulceration, as a result, does not often occur, and the incidence of dysenteric manifestations is corresponding small. When they are present, they occur late, and the prognosis, in the absence of prompt and adequate treatment, is always poor. Chronic dysentery is not the rule in patients who recover.

The incidence of malarial dysentery in this country after the war depends upon the possibility of the introduction of tropical or virulent malaria, which is discussed in another paper of this symposium. Naturally, the higher the incidence of this type of malaria, the higher will be the incidence of malarial dysentery, though at the most it will remain small.

Although the submucosa and even the mucosa of the intestine in kala-azar are infiltrated with numerous macrophages filled with *Leishmania* organisms, ulceration is unusual except in the terminal stages, and dysentery therefore does not occur in more than a small proportion of all cases. The rural incidence of kala-azar dysentery in endemic areas is estimated at 10 per cent and the urban at 1 per cent, differences in sanitary practices explaining the discrepancy. The explanation of dysentery is not clear, though some authors regard it as an intercurrent intestinal infection, such as amebic or bacillary dysentery. Since the chances of importation of a large number of cases of kala-azar are remote, the likelihood that dysentery of this origin will be of importance in the United States after the war is relatively small.

That the incidence of carcinoma of the intestine is increasing is well known. If, however, the concept should be established that the end-result of acute, and more particularly of chronic, dysenteries may be the development of malignant disease, this increase would be of great importance to the individual. It would mean, furthermore, that in the next two decades we may anticipate a rapid increase in the general incidence of intestinal malignancy, as the result of the high incidence of acute and chronic dysenteries among men in the armed forces.

Dysentery due to tuberculosis is extremely unusual and the etiology is clearcut, since it is usually associated with demonstrable pulmonary lesions. This was true in all three cases which I have personally observed.

SUMMARY

1. Because the armed forces of the United States are fighting today in every part of the world, the possibility exists that the diseases of every part of the world may after the war be introduced into every part of the country.

2. This possibility must be considered from both the individual and the epidemiologic standpoint.

3. The diseases which produce dysentery (in contrast to those which produce diarrhea) are limited in number, and the two most important, bacillary dysentery and amebic dysentery, are already prevalent in the United States. The introduction of more virulent types of bacillary dysentery is, however, a possibility. Both diseases are of individual significance, and bacillary dysentery may assume epidemic proportions.

4. Balantidial dysentery, though the causative parasite has a high incidence in certain animals, is apparently unusual in man except in the Tropics.

5. The remaining dysenteries, such as those associated with lymphogranuloma inguinale, nonspecific ulcerative colitis, salmonellosis and brucellosis, are not of general significance. Dysentery is only occasionally associated, usually in the terminal stages, with such diseases as malaria, leishmaniasis (kala-azar), and tuberculosis.

THE RICKETTSIA DISEASES; YELLOW FEVER; DENGUE AND SANDFLY FEVER

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NEW ORLEANS

Since I have been assigned a comparatively negative role in this symposium I shall make my contribution very brief.

My first assignment is rickettsia diseases. There have been between thirty and forty names given to the various rickettsia infections of man. In many instances different names have been given to the same disease, and in others the same name has been given to more than one distinct disease entity. Our knowledge of rickettsia disease is in its earliest stages and there is naturally a considerable amount of confusion; in the course of time no doubt the picture will be clarified.

In table 1 nineteen names of rickettsia infections are given. In several cases, even here, more than one name is given to what is obviously a single disease entity, and the table is by no means complete, but perhaps it contains all the more important rickettsia diseases. They are arranged in six groups. There are in a few instances some important cross relationships between members of different groups, but in each case, where there is more than one representative in a group, there is some strong epidemiologic, etiologic, or clinical tie between the various members of this group.

If you examine a map showing the world distribution of some of the rickettsia infections, you will notice that this war has already taken American soldiers into many places where these diseases are endemic. What are the chances of soldiers on their return bringing back some of these infections with them? It is possible that a soldier might return to this country during the incubation period and develop one of the rickettsia diseases after he arrived; this is possible but very unlikely in view of their relatively short incubation periods. However, the important point is, would such an incident be likely to introduce the infection to this country? Examination of the table will indicate that there is only one of these diseases in which the reservoir of infection is man, that is epidemic typhus. Epidemic typhus has been introduced many times into the United States and there have from time to time been outbreaks of the disease here, but none of importance within the last fifty years, and in view of the fact that louse infestation is very rare, it seems most un-

TABLE 1
RICKETTSIA DISEASES

Disease	*Rickettsia*	*Vector*	*Reservoir*
Epidemic typhus	R. prowazeki	Louse	Man
Brill's disease	R. prowazeki	—	(Man)
Murine typhus	R. mooseri	Flea: X. cheopis	Rats
Rocky Mountain spotted fever; Eastern and Western	R. rickettsi	Ticks: Dermacentor andersoni and variabilis	W. Mammals or Dermacentor
Sao Paulo fever	R. braziliensis	Amblyomma cayennense	Rodents
Tobia fever		Ticks	Rodents
Fièvre boutonneuse	R. conori	Dog tick: R. sanguineus	Rodents
S. African tick fever	R. pijperi	Ticks	Rodents
Tsutsugamushi disease or	R. orientalis or nipponica	Trombidial mites	Field
Japanese river fever		T. akamushi	rodents
Scrub or rural typhus		T. deliense	Rats
Sumatra mite fever		?	Rodents
New Guinea mite typhus		(T. minor)	Rodents
Queensland coastal fever		T. australiense	Rats
Trench fever	R. quintana	Louse	Louse
Australian Q fever	R. burneti	Ticks	Bandicoot
American Q fever	R. burneti (R. diaporica)	Dermacentor andersoni	?

likely that typhus would spread, even if it were introduced.

In the same group as epidemic typhus, Brill's disease is listed. Now Brill's disease is a sporadic and very mild form of typhus that has appeared in this country many times. There is considerable evidence that the rickettsia which causes it is identical with that of epidemic typhus, and the explanation given for these sporadic cases, which have almost all been in émigrés from European countries where typhus occurs, is that Brill's disease is a late release phenomenon in a person who has previously suffered from epidemic typhus.

Epidemic typhus is essentially a war disease. An outbreak has followed every great European war for as far back as historical records on the subject are reliable. After World War I there was an exceptionally severe outbreak, in which in Russia alone there were 4,000,000 cases in one year, and in Serbia, as Yugoslavia was called in those days, half the doctors in the country died of the disease. This war is unlikely to prove an exception; in fact already last year there was a severe outbreak in Egypt and North Africa, and reports indicate that there is an epidemic in Italy at present. True, all soldiers are inoculated against typhus, but the value of the vaccine has not been fully proved and it is possible that it modifies rather than prevents the infection. If Brill's disease is really a late relapse phenomenon of epidemic typhus, it seems possible that the future may bring forth a large number of such cases in soldiers returning from Europe.

Further, an incident has been reported from Ireland in which a box which contained clothes that had belonged to a typhus-infected family was incriminated as the cause of a small outbreak of epidemic typhus. It is thought that the infection originated from infected louse feces which had been shut up in the box for many years. This is not impossible, as rickettsiae remain viable for a very long time in the dry state, and, if this is true, it opens up great possibilities for sporadic cases in the post-war years. No doubt precautions will be taken to sterilize the soldiers' clothes, but such things as souvenirs may harbor the infection.

In the case of other rickettsia diseases, man is not known to harbor the infection for any length of time, nor is he likely to bring either the vectors or the reservoir hosts back with him. Furthermore, at least three of the groups have other representatives in this country already. One such disease is murine typhus; this was a rare disease in this country 25 years ago, but during the last two decades it has shown a progressive increase, and it appears to be extending its range. The two initial foci, one on the Mexican border and the others on the Southern and Eastern seaboards are tending to meet. This will be more evident when the data for the last few years are analyzed. The Southern states are primarily involved, but it has been reported from other states.

Rocky Mountain spotted fever, which is no longer confined to the Rocky Mountain states but has occurred in nearly every state in the union outside of New England, is another example. The distribution map, recently prepared by Faust, appears to suggest that this disease also is spreading. It is by no means certain that this is really the case, and it is possible that the map only indicates a greater awareness and a higher degree of diagnostic acumen on the part of the medical profession.

Finally, there is that very interesting disease referred to as "Q fever," which has also been called "nine-mile fever." At present this is more of a medical curiosity than a public health problem, but so was murine typhus twenty-five years ago.

It is not likely that new strains of any of these diseases will be brought in as a direct or indirect result of the war, nor are war conditions in any way likely to increase their incidence to any serious extent, but perhaps the revival of interest in tropical medicine that this war has initiated, will have as one of its results an increased interest in rickettsia infections generally, so that more attention will be paid to these tropical

—well, if not tropical, at least *exotique*—diseases already prevalent in this country.

Rocky Mountain spotted fever is usually a severe disease with a very characteristic clinical picture that includes an intense rash and it should be diagnosable clinically. Murine typhus and Brill's disease are milder diseases in which the rash may be absent, but a doubtful diagnosis can be confirmed by the simple Weil-Felix reaction with OX19 antigen, in the second week of the disease. The diagnosis of Q fever presents more difficulty. It usually takes the form of a pneumonitis. The diagnosis can also be confirmed serologically, though not in this case by the Weil-Felix reaction.

YELLOW FEVER

Again, this is a disease which should not be introduced as a direct result of the war, provided there is no relaxation of preventive measures. In the past, epidemics have from time to time occurred in the United States, but only one since the mode of transmission of the disease was understood, namely the New Orleans epidemic of 1905.

Most of the epidemics came and went befor the Stegomyia mosquito *(Aedes aegypti)* was known to be the vector. It must therefore be apparent that climatic conditions in the United States are unsuitable for the disease to establish itself permanently here.

For yellow fever to occur in epidemic form, there are three essentials: (1) the yellow fever virus; (2) the mosquito vector, and (3) a susceptible population.

Now, if the virus can be excluded from a country, or if the vector mosquitoes can be eliminated or reduced to a non-effective level, or if the population can be protected by vaccination, then the disease will not occur. The point of attack will depend entirely on the circumstances.

As you probably know, epidemiologically there are two types of yellow fever—the urban and the jungle types. In the former the source of infection is man and the vector is the Stegomyia mosquito; and in the latter the source is some jungle animal, as yet unidentified, and there are twenty or more mosquitoes that are capable of transmitting the infection.

In table 2 are shown the methods of control adopted in four sets of circumstances.

TABLE 2

THE CONTROL OF YELLOW FEVER

The relative importance of different methods in various circumstances

Method	Endemic areas: Urban	Endemic areas: Jungle	Non-endemic areas: Potentially endemic	Non-endemic areas: Climatically unsuitable
Exclusion of the virus	—	—	++	+
Elimination of the vector	++	—	+	++
Protection of man by inoculation	+	++	—	—

It is quite obvious that in the endemic areas one cannot exclude the virus; it is already established there in the human population or in the jungle reservoir. In an urban endemic center the main effort will be directed towards the elimination of the vector, but this would be quite impossible in a jungle area. Thus, in a jungle area we are left with inoculation of the whole population as the only possible means of prevention, and in Brazil and Colombia several millions of people have in fact been inoculated against yellow fever. This gives maximum protection for about four years, after which there is some evidence that immunity tends to decrease in certain persons. Of course, inoculation will be of value amongst a town population in an endemic area, but it should not be looked upon as the first and only line of defense as in the jungle areas. Further, many people will already be naturally protected by previous experience of the disease.

The case of the non-endemic areas is very different. Moreover, there are vast areas in Asia where Stegomyia mosquitoes abound. These are all potential endemic areas, and, if the virus once established itself there, it would seem that nothing could prevent a most disastrous outbreak. The virus could arrive either in a person during the incubation period, or during the first

three days of the disease, which might be mild or even symptomless, or in any infected mosquito. The measures that are taken in India, which is the western gateway to Asia, are aimed at preventing its slipping through in either. Everyone arriving in India from a yellow fever area must have been inoculated 14 days before he (or she) arrived in that yellow fever area, or he is isolated until nine days have elapsed since he left the last yellow fever country, whether he is a private, a field marshal, or a cabinet minister. As well as having to pass through anti-amaryl aerodromes en route, where preventive measures are taken, all airplanes are compelled to arrive at one airport in India and on arrival they are thoroughly de-insectized before anyone is allowed to get out. That is to say, the main aim is preventing the virus from entering the country, and, while anti-mosquito measures are also taken, especially near aerodromes, it would be impossible to keep the Stegomyia population of this whole continent down to a safe level, just as it would be impracticable to inoculate its thousand million odd inhabitants, so that these two measures are relegated to positions of secondary importance.

A map which shows that the main direct air routes from the United States to India pass through or near the worst yellow fever areas in the world also shows the proximity of the South American yellow fever to this country, but it does not by any means show all the air links.

The position in the United States is different: We are very near the endemic foci in South America, and therefore in some ways the danger would appear to be greater, but past experience has shown that the climate here is inimical to permanent yellow fever endemicity, though epidemics may occur.

With the endemic areas so near and with so many ports of entry, it would be impossible to be certain that no infected man or mosquito ever arrived in the country, so that the main aim has been to keep the Stegomyia mosquitoes at such a low level—a 2 per cent *Aëdes aegypti* index is usually considered safe—that if by any chance the virus did arrive again, the disease would not spread. Of course, very elaborate precautions are taken at all ports and air-ports to prevent infected mosquitoes arriving, but the strict regulations regarding inoculation that are applied in India are not applied here, and, although I believe the local health authorities are notified when an uninoculated person arrives from a yellow fever country within the incubation period, he is not isolated.

The increased air traffic resulting from the war of course increases the danger of a temporary return of yellow fever to the United States. To meet this danger additional precautions have been taken in many places, though I am told that the *Aëdes aegypti* index of New Orleans rose far above the safe level last fall, which is obviously a dangerous situation. All the army personnel are inoculated against yellow fefevr, but to extend this precaution to the civil population would be too drastic a measure in the circumstances.

DENGUE AND SANDFLY

These two diseases are related to one another in that they are both short fevers caused by filtrable viruses and are transmitted from man to man by insects. The differences are shown in table 3.

TABLE 3

Dengue	*Sandfly fever*
1. Virus present for first three days of fever.	1. Virus present day before fever and for the first two days of onset.
2. Transmitted by *Aëdes aegypti.*	2. Transmitted by *Phlebotomus papatasii.*
3. Eight days development in mosquito.	3. Seven days development in sandfly.
4. Mainly tropical.	4. Mainly sub-tropical.
5. Fever lasts five to seven days usually, sometimes less. Secondary rise of temperature occurs in 25 to 80 per cent of cases in different epidemics.	5. Fever lasts three to five days, usually, some times longer. Secondary rise of temperature rare.
6. Primary rash occasionally; secondary rash all over the body, in most epidemics.	
7. Immunity is variable and tends to be short.	

6. Primary rash rare.
7. Immunity is usually complete.

Dengue is today not unknown here, although epidemics have occurred previously. Increase in the traffic might easily lead to the re-importation of the disease from South and Central America, and, if the Stegomyias, of New Orleans, for example, are again allowed to get out of hand, an epidemic might well occur and cost this country's war plants some hundreds of thousand of man-days. Sandfly fever, on the other hand, is not likely to occur. There are few phlebotomi in this country and those that are present do not feed on man.

I have drawn as gloomy a picture as I can, and, while I do not believe that I have exaggerated the possibilities, I do not think that any of the diseases I have discussed, with the possible exceptions of yellow fever and dengue, are really very likely to provide either war-time or post-war problems to worry the medical profession, as undoubtedly will some of the diseases discussed by my colleagues.

HEMOFLAGELLATE INFECTIONS

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INTRODUCTION

From the protozoologic and pathologic points of view, it is very easy to trace the evolution of *Trypanosoma* and *Leishmania* diseases of man.

The most primitive in the evolutionary scale is a group of diseases caused by leishmanias, since the parasite occurs in the leishmania stage in the reticulo-endothelial cells of the vertebrate host and in the flagellate leptomonas stage in the sandfly and in culture. Therefore the primary pathology is one of reticulo-endotheliosis, while the parenchyma suffers only accidental and secondary changes.

The second group of diseases is African trypanosomiasis where the parasite lives and multiplies extracellularly in the blood and tissue fluids in the flagellate trypanosome stage, thus giving rise to primary pathology in the parenchyma of the viscera, mainly the lymphatic and central nervous system. Mesenchymal reaction is secondary. In the invertebrate host, the tsetse fly, and in culture media the parasite is in the flagellate crithidia and trypanosome stages.

The third group, which is the highest in the evolutionary scale, is American trypanosomiasis, in which the parasite multiplies in the leishmania stage in the parenchyma and mesenchyma cells of the various organs, while the blood forms are flagellate trypanosomes, and leptomonas and crithidia stages are transitory. The pathology includes both a reticulo-endotheliosis and parenchymal lesions. In the insect vector, the triatomid bug, and in culture the crithidia and trypanosome forms are produced. Thus, in this disease, the parasite goes through a complete cycle—leishmania, leptomonas, crithidia and trypanosome.

I. RETICULO-ENDOTHELIOSIS

1. *Kala-azar*

Visceral leishmaniasis or kala-azar which is produced by *Leismania donovani*, has a very extensive distribution. The Chinese type occurs mainly among children who are above five years and the dog is an important reservoir host. The Indian type occurs among adults and children, but no reservoir host has been discovered. Infantile kala-azar (the Mediterranean type) occurs among younger children and dogs. The Sudanese type occurs among all age groups. This is also the case in Argentina and Brazil, where the dog and cat are reservoir hosts.

Clinical Course: Kala-azar is a chronic disease which has an incubation period of two to three months or more, and is characterized by the gradual onset of fever recurring at irregular intervals, typically with a double daily rise of temperature every 24 hours. Progressively there is spleno-hepatomegaly, hypochromic microcytic anemia, leukopenia with monocytosis, edema of the skin, loss of weight, emasculation, diarrhea or dysentery, cachexia, granulopenia, dusky pigmentation of the skin, stunting of growth and intelligence, hemic murmur, hypoproteinemia with elevation of the se-

rum euglobulin level, a clean tongue, a good appetite and no jaundice, and death is usually due to an intercurrent infection.

Although any fever with or without splenomegaly must be considered in the differential diagnosis, the most important diseases which must be excluded are malaria, typhoid fever, Egyptian splenomegaly, schistosomiasis, Banti's syndrome and syphilis.

Laboratory Diagnosis: During the febrile stage thin and thick blood films stained with Wright's or Giemsa's stain may reveal the parasites in the mononuclear cells, while cultivation on the N.N.N. medium, and inoculation of hamsters are valuable supplementary tests. Examination of sternal bone marrow and splenic pulp is of particular value in chronic cases. The Napier aldehyde test, antimony test and Sia's precipitation test are relatively pathognomonic.

Treatment: The specific drug is antimony. Trivalent antimony salts, 2 per cent freshly prepared solution of tartar emetic or sodium antimony tartrate, injected intravenously, beginning with 2 c.c. and gradually increasing the dose to 5 c.c. Injections are given twice a week for a period of two to three months.

Fuadin or neoantimosan is given intramuscularly with an initial dose of 1.5 c.c. and gradually increased to 5 c. c. Fifteen injections are necessary.

Of the pentavalent salts, neotibosan is the most efficient. It is given intravenously with an initial does of 0.1 gram, which is gradually increased to 0.3 gram until 2.7 to 4 grams are given. Anthiomaline, diramine, stibamine glucoside, solustibosan and urea stibamine are also used.

Toxic symptoms due to the administration of antimony are cough, metallic taste in the mouth, vomiting, giddiness, delirium, rise and fall of temperature, cramps in the muscles of the calf, rapid pulse, colic, headache, arthritic pains and jaundice.

2. *Mucocutaneous South American Leishmaniasis, Uta or Espundia*

This is a chronic disease which is found in Latin America and is caused by *Leishmania brasilensis*. The known reservoir host are the dog and the agouti.

Clinical course: (a) *Cutaneous stage*. At the site where the sandfly introduces the parasite on the exposed parts of the body a macule appears, which becomes a papule, ulcerates, and on healing leaves a scar. This stage lasts for one to two years.

(b) *Mucocutaneous* or *metastic stage*: This develops around the nose or mouth after healing of the primary lesion. It is a destructive and ulcerative process extending posteriorly and destroying the soft parts of the nose as low as the pharynx and trachea, thus interfering with respiration and nutrition. Contraction of the tissues results in disfigurement. At times there is fever, anemia and pain in the affected parts. Complications are pneumonia and septicemia.

Laboratory Diagnosis: Smears of the lesion show parasites in the mononuclear cells. Culture on the N.N.N. medium, inoculation of the hamster and the Montenegro allergic skin test are also used.

Treatment: Antimony salts are specific. (See above.)

3. *Cutaneous Leishmaniasis, Oriental sore, Aleppo, Delhi or Bagdad Boil*

Clinical Course: This is a disease of the skin which occurs in certain parts of Asia, Africa and Europe, but is not co-endemic with kala-azar. It is caused by *Leishmania tropica*. Usually on the exposed parts of the body, two to 12 months following the introduction of the parasites by the sandfly, a macule appears, becoming a papule. With trauma it ulcerates and finally heals after nine to 12 months, leaving a disfiguring scar. Clinically the lesion is usually single, generalized, and abortive. Lymphatic, verrucous and lupus types have also been observed.

Laboratory Diagnosis: Smears of the lesion show the parasites in the mononuclear cells. Cultivation on the N.N.N., inoculation of the hamster, agglutination and skin tests are also used.

Treatment: For the preulcerative stage, atabrine infiltration of the lesion is recom-

mended; for the ulcerative stage, clean with hydrogen peroxide and apply sulfapyridine powder. In refractory cases systemic use of antimony, local application of CO_2 snow, berberine sulphate, or emetine hydrochloride may be needed.

Prophylaxis: Induce artificial boil by injecting living leptomonas from bacterially sterile cultures on the covered parts of the body. Immunity follows the healing of the lesion. Super-infection is possible, but reinfection does not take place.

II. PRIMARY PARENCHYMAL PATHOLOGY

1. *African Trypanosomiasis*

a. *Gambian Fever*: This is a chronic disease occurring in Africa between 15° N. and 15° S. of the equator, mainly the western and central parts. It is characterized by changes in the lymphatic and nervous systems. The etiologic agent is *Trypanosoma gambiense*.

Clinical Course: The incubation period is two weeks to a few months. The glandular stage begins with a trypanosome chancre which develops at the site of the bite of an infected tsetse fly, fever, erythematous rashes, edema of the hands, feet, eyes and joints, a generalized lymphadenopathy especially marked in the posterior triangle of the neck (Winterbottom's sign), and delayed reaction to pain (Kerandel's sign). Progressively the fever becomes very irregular and the patient shows asthenia, anemia, neutropenia with monocytosis, weakness, eye complications, and erythema nodosum. Death may result from intercurrent infection; but commonly it is followed in two to seven years after the initial infection by the cerebral or lethargic stage, due to the invasion of the brain by the parasites. The symptoms in this stage are tremors, headache, delusions, hysteria, mania, apathy, dullness, difficulty in walking, forgetfulness to masticate the food and loss of the deep reflexes. Progressively the gait is shuffling, the expression becomes vacant, there are drooping and edema of the eyelids, somnolence during the daytime and restlessness at night, paralysis, convulsions, rigidity of the neck, retraction of the head, bedsores, salivation, lethargy, loss of sphincteric control, hyperpyrexia, coma and death. Differential diagnosis must be made from malaria, kala- azar, pellagra, syphilis, leprosy and beriberi.

Laboratory Diagnosis: The parasites can be demonstrated in the blood by the thin and thick blood methods, and in lymph pulp and cerebrospinal fluid. The infection can be transmitted to mice, rats and guinea pigs.

Treatment: Tryparsamide, a pentavalent arsenical, is given intravenously with an initial dose of one gram and progressively increased to 2 to 3 grams at weekly intervals until a total dose of 24 to 80 grams has been administered. One hundred per cent cures may be expected if the nervous system is not invaded, but only 17 to 50 per cent cures if this stage has been reached. Bayer 205 (germanin) is also effective, and is given in 1 gram doses intravenously at weekly intervals for a total dose of 10 grams. Combined treatment is the most effective.

Toxic symptoms which often occur during the arsenical treatment are optic neuritis, dermatitis, hepatitis, albuminuria, headache, confusion, aphasia and coma.

b. *Rhodesian Fever*: This is a subacute disease occurring in East Africa 10° to 14° South of the equator, and is caused by *Trypanosoma rhodesiense*. It has a much shorter duration and graver prognosis in man and experimental animals than Gambian fever. There is no clean-cut distinction between the glandular and cerebral stages, but there is a marked typanosome chancre. The drug of choice is Bayer 205, which gives only 50 per cent cures if the central nervous system is not invaded, but is fatal once this stage has been reached.

III. RETICULO-ENDOTHELIOSIS AND PARENCHYMAL PATHOLOGY

American trypanosomiasis or Chagas' disease

This is a chronic disease of man in Latin America caused by *Trypanosoma cruzi*, but the parasite has been found in triatomid bugs and reservoir hosts in Texas, New Mexico, Arizona and California.

Clinical Course: The incubation period is one to two weeks. The acute form observed in children has a slow onset of high continued fever, with a slight morning drop, unilateral or less commonly a bilateral swelling of the eyelids and conjunctiva (Romaña's sign) at the site of the bite of the bug, a non-pitting mucoid edema, enlargement of the thyroid gland, spleen, liver, microcytic hypochromic anemia, leukocytosis and monocytosis, with 10 per cent mortality.

The chronic stage follows the acute form or begins as such in adults. The symptoms are very protean, depending upon the localization of the parasites. Cardiac, meningoencephalitic, myocardial, adrenal and ovarian types are described, with fever, anemia and leukopenia.

A differential diagnosis must be made from endemic, exophthalmic goiter, myxedema, hookworm disease and Addison's disease.

Laboratory Diagnosis: Thin and thick films of blood during the febrile stage show the trypanosome in the blood. Biopsy of lymph glands, lacrymal gland, and cultivation of infective material on the N.N.N. medium, xenodiagnosis, and inoculation into guinea pigs, rats and mice are also used. Complement fixation, agglutination and skin tests are also very helpful.

Treatment: This is symptomatic. No eminently satisfactory drug has been found.

It is probable that any or all of the hemoflagellate diseases may be brought back to the United States by returning troops who become infected in tropical areas where these diseases are endemic, but it is not likely that they will become established. Visceral leishmaniasis is present in several foci in South America and mucocutaneous leishmaniasis is widely distributed from Southern Brazil to Yucatan; but the chances of these diseases becoming established in the United States are relatively remote, since the sandfly vector is very restricted in its breeding grounds in America north of the Rio Grande. Since the tsetse fly, the vector of African trypanosomiasis, is present only in Africa, there is no possibility of this disease becoming established in the Americas unless the vector first becomes adapted to American soil. Apparently the environment factors are unfavorable for the tsetse fly in the Western Hemisphere, else this would have occurred years ago. American trypanosomiasis (Chagas' disease) is present in many of the Latin American republics and the causative agent, insect vectors and reservoir hosts have been found in the southwestern United States, but thus far no human cases have been reported in this country. This last infection is the only one of the hemoflagellate group in which autochthonous cases may be discovered.

FILARIASIS AND SCHISTOMIASIS

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FILARIASIS

Introduction: There are six commonly recognized filaria worms which infect man. Two species, *Acanthocheilonema perstans* and *Masonella* ozzardi, live in body cavities. They have embryos (microfilariae) which are "unsheathed" and circulate in the peripheral blood both day and night. These forms are not known to produce lesions and their infections may be regarded as essentially without symptoms. The loa worm, *Loa loa*, as an adult migrates through the subcutaneous tissues and from time to time crosses in front of the eye (i.e., under the corneal conjunctiva), producing fugitive swellings in its wake but otherwise causing no serious disturbance. Its microfilaria is "sheathed" and is more abundant in peripheral blood during the daytime than at night. A fourth species, *Onchocerca volvulus*, is immured as an adult in a fibrous matrix in the submucosa, most frequently on the head, neck, or at the junctions of the long bones. The microfilariae of this species do not enter the circulating blood but migrate through the cutaneous and subcutaneous tissues, especially in the lymphatic capillaries. They tend to enter the eyeball or optic nerve and are associated with a condition of diminished vision and eventual blindness.

Bancroft's filaria (*Wuchereria bancrofti*) and the Malay filaria (*W. malayi*)

live as adults in lymphatic vessels or nearby lymphoid tissues. They discharge "sheathed" microfilariae which get into the blood stream and circulate through the peripheral blood at night (that is, they have nocturnal periodicity). Because of the widespread distribution of these two filarias, their almost certain pathogenicity and their probable importance in the United States as a result of their importation in returning troops, these infections deserve special emphasis. Filariasis malayi produces clinical manifestations essentially the same as those caused by Bancroft's filariasis. Since the latter type is much more widely distributed in tropical war zones, it will be considered at some length.

BANCROFT'S FILARIASIS

Pathogenesis: There is a negligible skin reaction at the site where the mosquito intermediate host inoculates the infective-stage larvae, but as weeks go by there is from time to time an acute inflammatory reaction where the growing larvae temporarily block small lymphatic vessels or lodge is lymph nodes. Towards the end of the biological incubation period (about one to one and a half years after exposure) the adolescent worms tend to settle down in lymphoid tissue in the vicinity of the spermatic duct, the epididymis or the groin. Here they mate and the females discharge daily broods of microfilariae. Subacute cellular infiltration takes place around the parent worms but essentially no reaction is provoked by the circulating microfilariae. There is typically a recurrence of the inflammatory reaction around the adult worms, resulting in increased blockage of lymph flow. Eventually, as the worms become moribund, they are calcified and encapsulated in a fibrotic matrix. The fibrosis of lymphatic vessels and surrounding tissues gradually extends retrograde to the dying or dead worms, with ensuing varicosity of the involved lymphatics and frequently with elephantiasis.

Symptomatology: No symptoms develop immediately following exposure, but with the migration of the larvae into lymphatic vessels, their growth and the discharge of manifestations and later a fugitive lymphangitis, especially in the axilla, groin or vicinity of the external genitalia. Then there may be long periods of remission, but with the anticipation of recurrent attacks of lymphangitis with fever ("filarial fever"). Eventually varicose groin glands will develop, or a non-pitting elephantiasis of the genitalia or lower extremities. There may be chylous ascites, or chyluria, if a fistula or rupture occurs as a result of pressure within blocked lymphatics. Due to greatly diminished blood flow in the surface tissues of elephantoid areas, the skin cracks open, allowing pyogenic bacteria or fungi to gain entry, with the production of ulcers, abscesses or septicemia.

All of the above pathology may be produced within five years, but more frequently the development of the chronic picture of the disease requires twenty or more years.

Diagnosis: Suspected cases of Bancroft's filariasis give a history of having lived in endemic areas, with frequent exposure to the bites of domestic mosquitoes. They may have had one or more episodes of urticaria or other allergic manifestations and have had one or more attacks of lymphangitis, usually accompanied by fever. If the biological incubation period is still incomplete, microfilariae can not be demonstrated, but as soon as the worms become adult and as long as they are alive, "sheathed" microfilariae will be found in thick blood films (typically at night, especially between midnight and two a. m., but in the endemic South Pacific area at all hours of the twenty-four). In other patients the microfilariae may be present in urine (in patients with chyluria), in ascitic fluid (in patients with chylous ascites), or may be demonstrated in biopsied material or at operation. In the most chronic cases the parent worms will have died long since and microfilariae will not be found in circulating blood, but the visualization by x-ray of minute grape-like clusters of calcified granules in the center of the lesion at the head of a blocked and varicosed lymphatic vessel is pathognomonic.

Prognosis: This is good in so far as life

is concerned, but the eventual prognosis with reference to the development of chronic sequelae is poor.

Treatment: No satisfactory chemotherapy has yet been found to kill the parent worms, or more important, to reduce the chronic lesion. A modified Kondolean operation is temporarily helpful in reducing elephantiasis of an extremity but the condition usually recurs in about five years. Radical operation for elephantiasis scroti or varicose groin gland is frequently successful. Tight bandaging of an elephantoid extremity will usually be helpful in forcing blocked lymph into collateral channels and thus considerably reduce the elephantoid tissue. Sulfonamides or autogenous vaccines are useful in treating bacterial complications.

Prevention: Bancroft's filariasis is propagated by several species of domestic mosquitoes (*Culex, Aedes, et alii*), which breed in small household water containers or puddles of water near human habitations. Emptying water containers (cans, earthenware and glass jars) every four or five days and draining or filling low places where rainwater accumulates are measures of first importance, since the infection depends on mosquito transmission. Screening of homes and the use of mosquito repellents will minimize exposure of uninfected persons. Finally, infected patients, including carrier cases, temporarily asymptomatic but with microfilariae circulating in their blood, should be screened so that mosquitoes will not become infected. In proportion as these measures are diligently carried out the dangers of this disease will be reduced.

Several decades ago Bancroft's filariasis was widely endemic throughout the southeastern United States and until recently was present in the vicinity of Charleston, S. C. Today, it is probably no longer an endemic disease, but with the importation of many hundreds of cases in returned troops from the South Pacific areas, some of them at the threshhold of becoming transmitters, there should be an awakened consciousness of physician and layman alike, concerning the potential danger of domestic mosquitoes, such as was developed in New Orleans in 1905 at the time of the last yellow fever epidemic. War on domestic mosquitoes is always good prophylaxis, but is particularly good strategy at the present time.

SCHISTOSOMIASIS

Introduction: There are three species of schistosomes (helminths belonging to the Class Trematoda, family Schistosomatidae) which parasitize man. All of them inhabit venules draining visceral organs, hence the name "blood fluke." Two species, *Schistosoma japonicum* and *S. mansoni* live in the mesenteric venules draining respectively the small and the large bowel. They produce primarily intestinal and hepatic damage. The third species, *S. haematobium*, lives in the vesical plexus and produces lesions principally in the urinary bladder.

Migration and Maturity of the Etiologic Agents in the Human Body: Man is exposed to schistosome infection when he bathes, swims, wades or otherwise brings his skin in direct contact with fresh water containing the fork-tailed larvae (cercariae) of these flukes, which have previously undergone development and two-fold multiplication in certain species of freshwater snails. As the "infected water" drains off the skin, the larvae become attached, drop their tails, and digest their way down to the peripheral venules. In about twenty-four hours they enter afferent venous blood vessels and are carried through the right chambers of the heart to the lungs. They require about four days to squeeze through the pulmonary capillaries, are then carried through the left chambers of the heart and out through the aortic arch. The majority pass down through the thoracic and abdominal aorta to the mesenteric artery and pass through into the portal blood, where they lodge and begin to feed on whole blood. All larvae which become lodged outside the mesenteric system die and many produce petechial hemorrhages. Once within the intrahepatic portal system the larvae grow and in sixteen days (that is, about three weeks after skin exposure) are large

enough and strong enough to migrate out of the liver against incoming portal blood.

The young of *Schistosoma japonicum* get into the mesenteric venules draining the small bowel, mature, mate and the females begin to lay eggs about four to five weeks after skin exposure. Those of *S. mansoni* reach the venules draining the large bowel and egg-laying is initiated about six to seven weeks after skin exposure. Those of *S. haematobium* migrate down through the inferior mesenteric veins, pass through the hemorrhoidals or pudendals and reach the vesical plexus, where egg-laying begins about ten to twelve weeks after skin exposure.

Pathogenesis: This is divided into three successive stages: (1) the incubation period, (2) the acute stage and (3) the chronic stage.

The *incubation period* is initiated with the entry of the schistosome larvae into the skin. There is relatively little tissue reaction at the sites of penetration but an acute cellular infiltration occurs during passage through the pulmonary capillaries. Moreover, wherever the migrating larvae break out of capillaries or lodge in blind foci, they cause petechial hemorrhage. As the worms accumulate in the intra-hepatic portal vessels an acute periportal inflammatory reaction to the by-products of the developing worms occurs, indicated by an intense eosinophilia. These conditions approach a climax towards the end of the incubation period.

The *acute stage* is ushered in as the eggs, layed in the smaller venules in the muscular or submucous coats of the involved organs, work their way through the several layers of the organ into its lumen, with resultant traumatic and lytic damage to the cells. There is continued local and systemic reaction to the toxic by-products of the worms and their eggs, as evidenced in part by a profound eosinophilic leukocytosis.

The *chronic stage* almost imperceptibly succeeds the acute stage. In increasing numbers the eggs discharged by the female worms become temporarily lodged in the tissues and provoke the formation of abscesses which usually transform into pseudotubercles. These miliary pseudotubercles are from this time on the cardinal pathological processes and are centers for the development of fibroses, cicatrices and papillomata of the small bowel (*S. japonicum*), of the large bowel (*S. mansoni*) and of the urinary bladder (*S. haematobium*). Moreover, in the intestinal forms, but particularly pronounced in *S. japonicum* infection, the eggs escape into the larger mesenteric venules, are carried back into the liver and mesenteric lymph nodes and produce cirrhosis of these organs. With liver involvement the spleen compensatorily becomes greatly engorged and, as the hepatic cirrhosis proceeds, ascites develops. In the vesical type there is marked deposition of phosphatic salts in the bladder wall and uric acid crystals around eggs which are expelled into the lumen of the bladder. There is an occasional carcinoma of the rectum (especially in *S. masoni* infection) or of the bladder (*S. haematobium* infection). There is frequently a development of pseudotubercles in the lungs and involvement of the genitalia in the vesical type. Pyogenic infections may complicate the late chronic stage of *S. haematobium* infection. The leukocytosis of the acute stage changes to a neutropenia and monocytosis, but with a moderate eosinophilia. There is an increase in serum euglobin.

Symptomatology: The *incubation period* is initiated with a needling pain at each site of skin inoculation. There is a tendency to allergic states, particularly giant urticaria, first at the time when many larvae which have miscarried die in blind termini, and again as the toxic by-products of the growing worms become distributed throughout the system. Little by little the liver becomes enlarged and exquisitely tender. In the intestinal forms there are prodromata of late afternoon fever and night sweats, and a few days before the end of this period a rather profuse mucous diarrhea develops.

The *acute stage* in *S. japonicum* and *S. mansoni* is ushered in with intestinal discomfort, frequent desire to defecate and the passage of a dysenteric stool. In *S. mansoni* infection there is more tenesmus than

in *S. japonicum*. The patient is practically prostrate and goes to bed. This acute condition continues for two or three weeks, but with rest in bed it gradually subsides and the patient gets up, at times undertaking light work. With exercise the dysenteric condition recurs, so that only prolonged rest brings relief. In the vesical form the acute stage begins with the painless passage of blood at the end of the period of urination, but soon there is a burning sensation at times of micturition, bladder colic and the terminal discharge contains not only blood but purulent debris.

As the *chronic stage* comes on in the intestinal types there is increased digestive and hepatic dysfunction, leading to malnutrition and emaciation on the one hand and ascites and splenomegaly on the other. Moreover, the greatly enlarged spleen and mesenteric lymph nodes and the fibrosis of the mesentery push the diaphragm upwards, with consequent decrease in the size of the chest box and thus in the vital capacity of the lungs. In the vesical type there is incontinence with respect to the passage of urine, frequently complicated with bladder stone. Pyogenic infections may be sequelae to both the intestinal and vesical types of infection, but more frequently, the latter. Similarly, the chronic irritation of the fundus of the bladder tends to produce carcinoma of this organ more frequently than of the rectum, although prolapsus recti is not infrequent. Occasionally the vesical type secondarily involves the rectum, although it more frequently produces disease processes in the genitalia and the lungs. Death characteristically results from inanition, pneumonia or sepsis.

Diagnosis: Among natives in endemic areas it is rare to see schistosome infection in the incubation period or as a pure acute infection, usually because exposure over a period of years gives a picture of the acute state superimposed on chronic infection. Frequently the history of the patient is suggestive, that is, having lived in an endemic area, and having bathed in potentially "infected water," or having had episodes of dysentery, hematuria or bladder colic, especially after physical exertion.

During the incubation period giant urticaria may provide a lead or during the latter part of this period a tender, enlarged liver with a high eosinophilia may suggest a tentative diagnosis. Specific diagnosis must wait until the beginning of the acute stage, when the eggs are discharged in the stool, especially in flecks of blood and mucus *(S. japonicum, S. mansoni)* or in the urine, especially with blood and mucus in the last few cubic centimeters *(S. haematobium)*. If eggs are few in the stools, repeated sedimentation with decantation will be helpful in concentrating the eggs in the bottom sediment. In the vesical type the sediment from urine passed directly into an 8-ounce urinalysis glass usually contains the eggs of *S. haematobium*.

Prognosis: This is fair to excellent for cases with acute and early chronic infection, provided specific therapy is undertaken; always poor for late chronic stages with hepatic involvement or carcinoma.

Treatment: Antimony preparations are specific for all types of schistosome infection. Tartar emetic and sodium antimony tartrate are the salts most commonly employed intravenously. The former is the more stable preparation; the latter is better tolerated by the patient. Sterile solution of 2 to 6 per cent is administered intravenously three times a week, beginning with 1.5 c. c., then 3.5 c. c. and 5 c. c., and continuing if possible with the 5 c. c. dose until 1.35 gm. (20 gr.) have been administered (four weeks for 6 per cent solution, 12 weeks for 2 per cent solution).

Fuadin (stibophen) and anthiomaline are employed for intramuscular injection. They are more easily administered and better tolerated than the antimony tartrates but they less frequently produce a cure in one course of treatment. They are prepared commercially as a 6 per cent or 7 per cent solution and are given as follows: first day, 1.5 c. c.; second day, 3.5 c. c.; third day, 5 c. c., then 5 c. c. on alternate days or every third day until a total of 50 c. c. has been administered.

For cases with advanced hepatic cirrhosis specific therapy is useless.

Prevention: This should be planned in two ways, one for temporary exposure in an endemic area, the other for eradication of the infection.

Temporary protection requires that individuals or groups refrain from bathing or otherwise utilizing "infected water" (or water under suspicion of containing the schistosome larvae) until it has been hyperchlorinated, well filtered or boiled, or has stood for at least 24 hours in a snail-free container. Circumscribed bodies of fresh water under suspicion should be treated with copper sulphate (one volume for each 50,000 volumes of estimated water), to kill the snails and their schistosome cercariae. Natives should not be allowed to pollute waters within a mile of a campsite.

For permanent control provisions should be made for the sanitary disposal of all human excreta. This requires a long-time educational program to secure compliance of native populations. In addition, some reduction of the infection may be expected from subjecting snails in endemic areas to desiccation, quicklime or live steam, and from treating all infected persons with antimony.

Schistosome infections have never become established endemically in the United States, Mexico, Central America, Cuba or Jamaica, although many negro slaves brought in these diseases in past centuries. While the possibility of endemicity should not be excluded, the likelihood is scant. On the other hand, there is great likelihood that many cases of these infections will be brought into the country in returned troops, so that physicians should be cognizant of the clinical features of this disease group as well as of the potential dangers of establishing them in this country.

RECURRENT MALARIA IN MILITARY PERSONNEL

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Malaria will probably be one of the great medical problems of the general practitioner after the war. Soldiers, sailors, marines, and civilian employees who contracted malaria in tropical and subtropical areas will be returning to the United States as carriers and recurrent patients. These people will, therefore, be a potential source of various tropical strains of the malaria plasmodia. Civilian practitioners of medicine may be called upon to treat these individuals. It is of utmost importance that these physicians be familiar with the symptoms and be alert to diagnose and treat correctly these patients so as to prevent the spread of malaria. It is possible that local outbreaks of malaria may occur in this country, starting from relapsing cases acquired abroad. The United States Public Health Service recognizes this possibility and is carrying out intensive anti-mosquito programs. Physicians can aid by early diagnosis, by reporting of cases, by adequate treatment and by mosquito control. It is well known that the anopheles quadrimaculatus mosquito is present in Louisiana and is therefore of particular importance to local physicians. Great care should be used to see that all patients with malaria, including those with relapses, be protected from mosquitoes by a bed net or be treated in a ward made free of mosquitoes by chemical means.

Relapses are characteristic of all types of malaria but are particularly prone to occur in cases infected with the strain of plasmodium vivax acquired in endemic South Pacific Islands. It is not unusual for a patient to have ten or more relapses.

Relapses may occur without obvious cause but are most apt to follow any condition that lowers body resistance, such as exposure to cold, alcoholic, dietetic, or venereal excesses, intercurrent infections, a serious accident, a surgical operation, childbirth, or exertion of routine military life.

A relapse may occur after a remission of six to eighteen months. One reason why relapses occur is the fact that many cases of

malaria are not adequately or completely treated during their initial infection. The parasites become lodged in the organs and tissues of the body, especially in the spleen and bone marrow where they are further protected from drugs. It is generally believed that relapses are due to a failure of the defensive forces of the body to restrict the multiplication of the parasites to negligible proportions, as they do during the latent stages of infection.

There is no known drug which will prevent relapses. Until some drug is discovered which will attack the sporozoites before they continue their life cycle the likelihood of recurrences is probable.

Quinine, atabrine and plasmochin are the drugs most commonly used for treatment. Quinine and atabrine act on the schizonts and trophozoites of all phasmodia affecting human beings. Plasmochin, a quinoline derivative, acts primarily on the gametocytes (the sexual forms). All three drugs are however alike in their inability in a certain number of cases to cure permanently, that is, without the occurrence of relapses. They also fail in safe doses to prevent maturation of the merozoites.

The treatment which we are following at the Naval Hospital in New Orleans is the combined quinine, atabrine and plasmochin plan recommended by the Subcommittee on Tropical Diseases of the National Research Council. The plan is as follows:

1. Quinine sulfate 0.64 gm. (10 grains) three times daily after meals until pyrexia is controlled.

2. Then atabrine dihydrochloride 0.1 gm. (1½ grains) daily after meals for five days.

3. Two days of no antimalarial medication.

4. Then plasmochin 0.01 gm. (3/20 grain) three times daily after meals for five days. Discontinue if toxic symptoms appear. Never give atabrine and plasmochin concurrently.

It is extremely important that physicians be aware of falciparum infections since they are prone to cause cerebral symptoms and may even terminate fatally. The symptoms may be so obscure that malaria is not suspected and coma or even death may occur before the diagnosis is made. It is therefore essential that adequate and early treatment be instigated. Clinically, malaria should be suspected in any person with any complaint whatever if that individual has recently returned from the Tropics. Repeated smears should be made before a case is not considered to be malaria.

The following case is presented to illustrate some of the points brought out in this discussion.

CASE REPORT

I. M., ship's cook 2nd class, U. S. Navy, age 22, of New Orleans, states that when he left the United States in March 1943 he started to take atabrine daily under the supervision of a pharmacist's mate as suppresive treatment. He was first taken ill with malaria in Guadalcanal on June 16, 1943. He had symptoms of malaria for three weeks before his condition was definitely diagnosed. At that time he complained of headaches, chills and fever. On July 20, 1943 the plasmodium vivax was demonstrated on blood smear and according to his health record he was given quinine 2 grains every four hours a day and night for three days, along with atabrine gr. 1½ three times a day. After a rest of two days, plasmochin gr. 1/3 was given every night for five days. Despite this treatment he still continued to run a fever of 101° or more.

On August 29 smears were still positive for plasmodium vivax and 6 grains of quinine was given daily for 14 days. On September 18 smears were negative although he continued to run an occasional temperature up to 100°.

He was evacuated to the United States and on October 5 was admitted to the U. S. Naval Hospital, Oakland, California. At that time it was noted the patient had been complaining of chills and fever every two to three weeks and that smears for malaria remained positive. Physical examination showed the patient to be well developed but somewhat undernourished, with a weight loss of 25 pounds. The spleen was palpable, one finger below costal margin.

A smear on October 8 was positive for malaria (plasmodium vivax). He was again treated with quinine and atabrine, along with bed rest. Following this he was given quinine, 10 grains twice a day, and sent to the Convalescent Home at Santa Cruz, California on November 16. After being there for a month he was given a convalescent leave. While at home he had another chill and at this time he took 30 grains of quinine for two days. He was admitted to the U. S. Naval Hospital, New Orleans, on January 3, 1944, having

another chill and temperature up to 103.2°. Smear was positive for plasmodium vivax. He was now given quinine, 6 grains three times a day, for five days and then quinine 6 grains with plasmochin gr. 1/6 three times a day, for five days.

Since being in this hospital he has had two more relapses with positive smears. With his last relapse he was put on the combined quinine, atabrine and plasmochin regime outlined previously. For over two months now he has been symptom free and his general health has improved.

SUMMARY

1. This case shows that this individual developed malaria despite the fact that he was taking suppressive treatment under careful supervision.

2. Treatment failed to prevent the occurrence of relapses and this patient has had 15 to 20 relapses in a period of about six months.

3. Quinine, atabrine and plasmochin given by the method suggested by the Subcommittee on Tropical Diseases of the National Research Council seems to be the most effective plan of treatment.

THE PATIENT-PHYSICIAN RELATIONSHIP*

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The patient-physician relationship is something many of us take for granted and to which we give little thought, particularly to the psychodynamics involved. Yet there are few, if any, professional men of clinical experience who will deny its profound importance. Perhaps one of the best ways to reach an understanding of what precisely is involved in this relationship, is to approach it through historical perspective.

This relationship is an ancient one, possibly one of the oldest to be recorded and catalogued in the chronicles of human experience. Certainly, it can be traced back to the medicine man of tribal life, and whether we like it or not, we are direct descendants of this worker of magic. While incantations, thaumaturgy, and rituals, operating through fear and wonderment in his subjects, he wielded a potent authority over their minds by investing herbs, amulets, and charms with special power, thus using the well known principle of indirect suggestion. He was only too often a successful therapeutist. His methods, however, encouraged uncritical attitudes so characteristic of primitive, pre-logic thinking.

As medicine moved down the centuries, with a shifting from magic to mysticism, the high priests of each respective civilization took over to a large extent the responsibility for the sorrows and sicknesses which beset their flocks. Finally, time brought Hippocrates, who delivered medicine from much of its magic and some of its superstition, and by emancipating it from theologic restrictions, gave impetus to its development as a discipline in its own right. Time again was kind when it molded a man of unusual qualities, unselfish, indomitable, consecrated to the alleviation of human suffering, *the family physician.* This man held a big place in the hearts and lives of his patients in a society built around strong paternal figures. He was deeply respected in his community, not only as a good doctor, advisor, and friend, but as a leader of civic action and thought. Often he was a poor business man who neglected to collect money for his services or invest what he had with shrewdness, but generally he reaped bigger rewards in successful healing. His relationship with his patient was vested in authority, but his opinions were tinctured with humility, and his advice with benevolence and understanding. In the America of those days, transportation was difficult, and small community life prevailed. But no little farm was too distant to be inaccessible to the doctor and his horse. The life of an old patient waiting upon his skill, or a new baby to be brought into the world as he had brought the father before him, was an imperative call. He was the mainspring of community life, servant and confessor to

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all, a real sociologist and philosopher, and a keen student of human nature. All the gossip of his little world came to his ears, and he never became too detached from it to lose sight of his patients as people, instead of walking disorders. The city doctor of this era also shared this viewpoint of treating the man rather than his complaint, and similarly played a part truly paternal in the lives of his patients. Professional reserve was maintained by writing prescriptions in Latin, and medical matters were discussed sufficiently to meet the patient's therapeutic needs and allowed to go at that—a method still effective today. Every great discovery in medicine was not given out in scientific detail, to be garbled by popular publications, on the premise laymen must be completely informed. He knew too much information could bewilder, confuse, and create more symptoms. The point is, that he kept much of his therapeutics and many of his tricks to himself. He knew that logic was better than magic, but he did not deceive himself by thinking people reason, when mostly they rationalize; by thinking people use science when mostly they use supposition.

When we entered upon an era of rapid transit and streamlined treatment, the family physician lost his unique place. Clinics and cliques entered the picture, bringing much that was good, but also losing much that was valuable along the line. We became intoxicated with the scientific method. We broke man into segments. We dissected him, we put him under the microscope, we took pictures of his functions and subfunctions, on and on, with the yen to break him down into miniscules of matter: veritably a pedagogical quirk devoid of holism, respect for the laws of biology—essentially a progressive dehumanizing of man. I would add, however, that I have no quarrel with science, merely with the manner in which it is used and abused.

Fortunately, through the period when the family physician was losing his place, the psychiatrist, in spite of medical bigotry, began studying and treating man as an individual, living in a social and cultural milieu. He thus came to appreciate the necessity for establishing and maintaining a working relationship between his patient and himself. The fact that he had to work with disordered personalities, created problems for which he found new solutions through the study of the patient-physician relationship, which in turn led to an understanding of its psychodynamics. Thus he should be credited with the discovery of its real significance, and medicine can be grateful for his fearless observations made early in the century. Previously no scientific effort had been given to a frank analysis of human relationships, but rather they were left to the poets and romanticists; psychiatrists, however, made them the province of the physician.

I would like to mention a few of these. Beginning with the relationship of the one to the many, we find lecturer and audience, captain and company, leader and mob, Hitler and henchmen. Relationships with a strong sexual component add parties to an engagement or marriage, crushes, homosexual affairs, and the mercenary one between prostitute and patron. Less lurid is simple acquaintance and friendship, employer and employee, and on a professional level, we find teacher and pupil, lawyer and client, priest and parishioner, and finally, the physician and his patient.

This relationship begins when the patient makes his decision to consult his doctor. It becomes a concrete reality when he lays eyes upon him for the first time, and may well have received a bias from the handshake, manner, or address used by his physician on this occasion. We must remember this patient-physician relationship is highly charged with the imprint of centuries which have slowly conditioned both parties to expect certain things of each other. The physician is expected to be a man of learning and experience, dependable, understanding, and motivated by a strong sense of responsibility. What in turn do we expect from our patient? A person possibly more informed and critical than his forefathers, conditioned by a highly intellectualized environment, yet suggestible

as man always has been; one torn by hope and fear, yet amenable to treatment in the setting of a healthy doctor-patient relationship, in which there is sufficient emotional detachment to avoid personal involvement.

This relationship takes place in a framework of formality and propriety, actually functioning in the medium of conversation, which is skilfully directed by the physician as a rhetorical - logical process. Thus through ideas are made analyses, interpretations and syntheses, concepts and attitudes are exchanged, advice and suggestions are given. It has been said that "Words are like magic." They are at once the weapon which the physician uses to combat virulent ideas fermenting in the mind of his patient and the wedge to introduce a more benign strain therein. For malignant bacteria at work in the body are not more deadly than poisonous ideas within the mind, or multiplying in a society with whose customs and regulations one is at odds. On the other hand, wholesome ideas properly introduced and incubated, contribute to therapeutic success.

Beneath the flow of tendentious conversation between patient and physician, move the emotional processes, carrying positive and negative forces which strengthen or sever the relationship between them, and more than all else, hasten or retard the patient's recovery. For example, these emotions may be associated with unpleasant events and experiences, may contribute to the making of strong attitudes toward life and an earnest wish for recovery, or paradoxically, they may perpetuate his symptoms and lead him to evade diagnosis. Emotional processes were at one time man's most effective means of communication and adjustment, particularly when his language was unverbalized and consisted mainly of hoots and howls, squawks and squeals, crows and cackles. They are still at work today, giving color and meaning to his rhetorical - logical processes, integrating them with the organ systems and organs into "total" functions, or behavior, determined by his environmental needs of the present, with conditioning from the past and with anticipation for the future. Blending with these processes, the most potent, the most primitive, and the most barbaric forces of all, lie in wait for an opening—the instinctual processes, demanding realization of life's fundamental biological principles. We then have at our disposal and co-temporaneously in operation, this whole gamut of man's mental processes focused to symbolization in consciousness while we are engaging him in conversation for clinical obeervation and study. Hence we see that an appeal to all these components cannot be neglected by the astute physician, for the freeing of these emotional forces may loosen or completely alleviate his symptoms. In the emotional process is found, moreover, the catalyzer which will promote an effective relationship smoothing the path to therapeutic success.

Of greatest moment is the physician's personality. He will become increasingly aware of the importance of acquiring such social assets as tact, amiability, composure, and sincerity, discreetly seasoned with a dash of kindly humor and reserve. Above all, he must train himself to become a constructive listener. Time must be given the patient to ventilate his troubles, while skilfully guiding him in order to extract much valuable information without his being aware of it, *thereby getting the story behind the story* without brusque cross-examination. The doctor must never give the impression he is too busy to listen, and in a hurry to dismiss the patient, pressed as he may be for time. He thus courts the emotional cooperation of his patient thereby fostering a smooth, effective *esprit de deux*.

Such relationship once established, characterized by an emotional attunement between them, is called "en rapport" or "rapport." It means oneness in thought and action; a co-participation in mutual assistance and understanding; an understanding directed toward the essential goal of recovery in the one who is sick. Clinical experience teaches us that quick appraisal of the patient's emotional make-up and his attitude towards his illness, therefore, should

be one of the first things to ascertain. Whether his disorder be organic, functional, or a mixture of both, comes to the same thing when he is being treated as a person who is sick. What matters is to understand his emotional functions in order to use them consistently throughout the therapeutic relationship in diagnosing, treating, and managing the person and his disorder through his recovery and readjustment to life.

There are various theories about the emotional bond between the patient and his physician. For instance, the Freudian thinks of it, not as "rapport," but as "transfer." By this, he means that the patient transfers his love and affection from his primary love object to the physician: the physician playing the role of father, mother substitute, etc. Here the physician must be careful not to become emotionally involved with his patient while playing a therapeutic part, and at every stage have in mind the eventual weaning of the patient from himself as love-object, and diverting the famous Freudian libido, to socially suitable persons. Adler, another prominent psychiatrist, took this same libido, gave it a Nietzchean twist into the will to superiority, which must be pruned to decorous dimensions or induced to grow to adequate stature. The skilful psychiatrist can be helpful in both instances. Jung was intrigued by the unplumbed depths of man's collective unconscious and the powers residing therein. Here he found enormous historic and aesthetic content which incited the libido to play versatile roles. He traced man's psychic evolution through the ages as others have traced his physical evolution. He uncovered the source of mythology and showed that even now gods and devils walk the earth in the shape of archetypes within one's unconscious mind. Certain archetypes were to be traced in all men, which had slowly evolved through experiences common to the race in its slow evolution. To Jung, one might be the idea of the physician, for example, and a less ancient one stemming from this, the family physician. Whenever a human being approximates one of these archetypes, he fixes upon himself the unconscious love or hatred which the archetype itself provokes. Such a figure is Hitler, who has crystallized the fanatical devotion of a people who love the tyrant archetype, and the hatred of those who reject it.

The psychiatrist who borrows from the different "schools" their valid teachings and uses them with a middle-of-the-road technic, might be considered an eclectic: he avoids bias and tenetical restrictions, neither exploits the patient for his own research, nor holds him under treatment for ransom. A similar therapeutic procedure is the best one for the general physician who is working in a framework of many human diseases and disorders, meanwhile maintaining through successful rapport, a working relationship with his patient.

The art of medicine can never dispense with these principles of psychotherapy, they should be known by every physician, regardless of his field of work, and are not too difficult to assimilate if he will devote some time and effort toward acquiring their theory and technics. After all, these fundamentals of psychotherapy are nothing more than a means of handling those who are disturbed, disordered, or diseased, and are not to be thought of as hocus-pocus, or spoken of derisively as "boloney." Rather psychotherapy is a legitimate part of the art of healing. Foremost for its application is a sound, smooth patient-physician relationship, something about which all the different "schools" agree.

We have seen that it has evolved through centuries of mutual experience uniting layman and doctor. It is something of which we may well be proud and should guard at all costs, since our patients confide to us things which even a devout Catholic conscience would not yield to his priest. Pause and think about this. . . . It indicates the great faith society holds in us as professional men. It is protected by law in every land, with the possible exception of fascist countries. It has been given the near sanctity of a true family tie, filial and dependent on the one hand, paternal and protective on the other, only broken in those

countries which have attempted to stamp out family loyalties and substitute the supreme welfare of the State. Yet I feel safe in predicting that the ancient relationship will survive this war, cherished by the democracies, and will be the first right restored to the vanquished enemy lands, once the war is over.

It is my humble opinion that the profession has become conscious of this relationship through speakers and writers of the day. In this era of scientific awareness with its shiny toys and gadgets, somehow we lost sight of the true nature of man, and departed from the essentials of healing. Certainly, a more careful appraisal of it is paramount in both teaching and practice. It is high time that medical education bring itself to the task of promoting an earnest effort towards a full and unbiased appreciation of it throughout the medical student's tenure and contact with his faculty, and widen the opportunity for a curriculum in which reposes more time for instruction in the fundamentals of the psychology of this relationship. In times such as these, it is utterly microscopic and mentally myopic to scoff at psychiatrists when they are progressively giving more meaning to this relationship, with all its implications in a society of which we as professional workers constitute a group. We are all uncomfortably aware of incursions into this relationship upon the part of people outside our profession, who operate under the guise of service to humanity, and feel divinely appointed to assume obligations evaded by too many of our colleagues. Thus it is obvious to all of us with socialized medicine in the offing, that we should undertake individually and collectively a fuller appraisal, enhancement, and use of this relationship. Socialized medicine may in part be the expressed dissatisfaction and confusion of a people who deserted the family physician for the specialists, and now wonder how many specialists it takes to make a good doctor.

Apparently there has never been a greater need for fine doctors. To the average patient this means those who understand and use the opportunities that lie in the doctor-patient relationship. For they feel that within it, and deriving from it is the amelioration and solution of many of their personal and social ills. In fact it may be said to be the basis and bulwark of all treatment. Therapy starts and ends with the relationship, regardless of what is done in the interim, and as long as human beings seek health and happiness, and fear disease and disorder, this psychological tie between them and the doctor of their choice, may not be lightly dismissed as irrelevant and immaterial either in the medical schools or in actual practice.

Minds are being bombarded by conflicting ideas and propaganda over the air, on the screen, and in the press, associated with which are the natural tensions born of the highly competitive life in a war-torn world, and whatever our profession can lend toward the stabilization of the individual living in this world will be deeply appreciated by society at large. Our profession is one dedicated to the whole man, not merely to his organs and his functions; to his social welfare, not merely to his health. Our duty then, is to conceive of man as a social being, a spiritual being, a mental being, and physical being, but above all, a *human being!*

DISCUSSION

Dr. C. S. Holbrook (New Orleans): I think Dr. Watters has brought to us in a very scholarly presentation a most important relationship with which we are all somewhat familiar. I do not know of anything more important to the welfare of our patients than the proper rapport between the patient and physician. We might be almost criticized for bringing this subject to a group largely made up of this type of therapist, the family physician, whose value is, in large part, due to his interest in the patient as a whole and not as a conglomeration of parts. His value also depends upon the feeling that the patient has toward him as a healer and helper. Psychiatry largely depends on interpretation of these emotional reactions and proper directing of them. We have come to do it by training. The family physician has learned to do it from practice and inherent qualities that he has and his value depends largely on that.

Unfortunately medicine has developed into specialties, reducing this very important aspect of treatment because the specialist examines one part of the patient—eye, nose or throat or for ortho-

pedic conditions or determines how his gastro-intestinal tract functions—and has very little time for anything else. Quite frequently we find that this type of examination reveals a perfectly normal individual yet this individual is ill and what he is looking for is an opportunity to get rid of his fears, his tension state, and in the past that has often been accomplished by the general practitioner or family doctor. This can be done today and is being done today. The specialist can and is doing it today. A waiting room full of people is certainly a detriment toward anything approaching psychotherapy. The most important interview with a patient is the first interview. They often unload their difficulties and problems and various relations at that time better than at any other time. If a physician is fortunate enough to give an hour or an hour and a half to such an interview he will be practicing splendid psychotherapy. The difficulty is to find the time, however we should, in our various specialties and contacts with the patient try to find out more about the instinctive and emotional make-up of the patient and in that way many difficult problems will be simplified.

Dr. J. H. Musser (New Orleans): I hardly know what to say on this very interesting subject that Dr. Watters has presented so well. I rather thought that his talk was going to be on somewhat different lines than it was.

What he has said, I think, is extremely worthwhile and certainly is something that gives us food for thought. There is no doubt at all that the patient-physician relationship is extremely important and that there are some doctors who can get "en rapport" very rapidly and promptly and those are the succesful men in their positions. We, as teachers, can not teach this to students. I think it is something that they have to learn themselves and has to be engrained in a man or he is not going to be a successful practitioner of medicine.

I have seen this exemplified in following careers of boys graduating from our own medical school. Men who are AOA men—in the first ten of the class, with magnificent scholastic records—who are not as successful as men in the lower third of the class, in the practice of medicine. They do not understand the need and importance of getting the point of view of their patients and understanding their patients and working with their patients as a team. I wish that we as teachers would teach the students how to approach the patient properly and how to express to that patient sympathy for his troubles and make the patient feel that there is a "God Love" as Dr. Watters said, and to make the patient feel that we are there to help him. You will appreciate that this is the psychologic, in contradistinction to the physical care of the sick individual.

Dr. L. Roland Young (Covington): I feel Dr. Watters has given helpful ideas in this most important and interesting phase of medical work. It was Dr. Wier Mitchell of Philadelphia who was so strinkingly successful because he treated the person as well as the disease. This was during the latter part of the last century and he became world famed.

This relationship must be as direct and as simple as possible for best understanding and cooperaiton. The objective must be kept clearly before the mind of the patient and mutual interest aroused. We must not overlook one important thing in this matter; it has been shown or proved that our anticipatory life affects our behavior more so than does our immediate situation, so when practical give assurance of recovery.

Dr. T. A. Watters (in closing): I am indeed pleased with the comments of my discussors. They are very kind. I wish to re-emphasize the first interview; get a wholesome amiable start. I would like further to re-emphasize the importance of emotions. Really that is what we do with our patients: we work with their emotions, and the disorders they produce.

I appreciate Dr. Musser's remarks. I am in agreement with him about AOA students. We can teach a student technics and theories but we can not supply him with what his home failed to give in the way of good breeding. I think there is much the medical student can learn in his home as far as being a gentleman and handling people with finesse.

I am glad that Dr. Young agrees with me about a friendly manner in helping patients being most important.

I hope in this paper I have brought before you something which certainly, in my opinion, is timely and which today cannot be given enough consideration.

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SYMPOSIUM ON INTENSIVE METHODS OF TREATMENT OF EARLY SYPHILIS*

THE COMBINED USE OF FEVER AND CHEMOTHERAPY IN SYPHILIS

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Probably the first reference to an intensified method of treatment for syphilis is found in the "Autobiography" of Benevenuto Cellini, in which the author refers in glowing terms to the benefits accruing to him from an attack of malaria, which,

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he alleged, cured the Morbus Gallicum that he had contracted from a serving maid. It was in the next century that Sydenham said, "Fever is a mighty engine which nature brings into the world for the conquest of her enemies." There was, however, no application of this idea for the next 200 years.

In 1887, Wagner von Jaurreg published his first observations relative to the effect of high temperature on the course of central nervous system syphilis. He continued his work on this phase of treatment for approximately thirty years, and laid the foundation for the researches into the effect of fever on both *T. pallidum* and its hosts, natural and artificial. In the late 1920's, Bessemans of Belgium began to investigate the effect of fever on the causative organism of syphilis, and in 1933 and succeeding years he published articles in the American literature, dealing with the thermal death point of *T. pallidum*, and the effect of various types of artificial fever on laboratory animals and man.

Bessemans' first report in the American literature[1] was to the effect that high temperatures, whatever the mechanism of induction, killed *T. pallidum* without serious injury to the host, and in 1939 he[2] published a study in which he came to the conclusion that a temperature of 42° C. (107.6°F.) maintained for one hour, or of 40°C. (104°F.) for two hours, would kill treponemes in external lesions of primary and secondary syphilis. This work was done on rabbits with experimental syphilis, fever being induced by hot baths or the inductotherm, and the results checked as to disappearance of treponemes from the lesions, healing of lesions, and the results in attempts at transfer to other animals.

Further work, however, by Boak and his co-workers[3] indicated that the thermal death time for *T. pallidum* was, in contrast to Bessemans' findings, 46°C. (114°F.) for one hour. In support of this, the data on fever therapy of early syphilis by Epstein[4] in 1935 revealed that of thirty-one patients with early syphilis treated by fever alone, 10 per cent had clinical recurrences within a short time, and none became sero-negative after one or more sessions of fever, up to 105°F. of three to six hours' duration.

A further attempt was made (Boak, Carpenter, Jones, Kampmeier, McCann, Warren and Williams) to treat early syphilis by fever alone with prolonged sessions of fever (9-15 hours) at temperatures ranging from 105-106°F. Eight cases of darkfield positive, sero-positive, primary and secondary syphilis were treated. Of this number, five were followed closely and four underwent clinical relapse. Of the remainder, all were found to have remained sero-positive, and had been placed on chemotherapy by other physicians or clinics. It was noted, however, that all cases became darkfield negative after five hours of fever, and that the initial lesions healed rapidly. In the follow-up studies, it was found that all remained sero-positive, and that some patients demonstrated a nincrease in the titer of their serologic tests.

Similarly, Simpson, Rose and Kendall[5] began a study, in the course of which they intended to treat 25 cases of primary and secondary syphilis by fever alone, given in 10 weekly sessions of five hours each, with temperatures of 105-106°F. They treated eight patients, but found relapse so frequent that the project was abandoned.

The same workers[5] had, since 1932, carried on studies of a combined fever and chemotherapy schedule in early syphilis, in which each patient received fever and arsenical therapy over 10-20 week periods, together with an injection of bismuth at each fever session. This series comprised 27 patients, who received weekly or biweekly fever, together with neoarsphenamine and bismuth. Of these patients, followed for four or more years, none has shown evidence of clinical or serologic relapse.

It is of interest to note that no patients developed arsenical dermatitis while receiving this type of combined treatment. One patient with early syphilis included in this series had developed exfoliative dermatitis from neoarsphenamine administered prior to his experience with pyreto-

chemotherapy. When given a test dose of 1 mg. of the same drug, he again developed dermatitis, but following recovery from this episode, was given fever, and while in the fever cabinet was again given the same dose of neoarsphenamine. No dermatitis developed. Additional treatment with bismarsen during fever did not produce untoward results.

In 1942, the same workers[5] published data on 23 patients treated by a one day combined pyreto-chemo-therapeutic method. Each patient received a ten-hour session of fever, with a temperature of 106° F., receiving an injection of 0.2 gm. of bismuth subsalicylate immediately preceding the fever. An arsenical (mapharsen) was then given in three 60 mg. doses every three hours, the first being given at the time a rectal temperature of 106° F. was obtained. Mild jaundice was the only complication of treatment. All these patients were followed from six months to two and a half years before the study was published, and none developed clinical or serologic relapse in this period.

The longest series of cases which has appeared in the literature to date is presented by Bundesen, Bauer, and Kendall.[6] These patients were all treated in the Chicago Intensive Treatment Center. The treatment at present consists of the administration of 1.76 mg. of mapharsen per kilo of body weight, with a maximum of 180 mg. regardless of weight, in three equally divided doses. In addition, 0.26 gm. of bismuth subsalicylate is given intramuscularly within 24 hours preceding the beginning of fever. The arsenical is given according to the plan originated by Simpson, Rose, and Kendall. Fever is maintained at 106° F. rectally for eight hours.

Pre-treatment examination consists of a complete physical examination with special attention to the cardiovascular system and lungs, x-ray examination of the chest, electrocardiogram, lumbar puncture, blood count, sedimentation time, urinalysis, and determination of the icterus index.

The total number of patients to date of publication was 931.

The first 13 patients received treatment as just outlined, save that the dose of mapharsen was 120 mg. The thirteenth case terminated fatally, and, though postmortem examination revealed an extensive miliary tuberculosis, the dose was lowered to 60 mg. In this case, the calvarium was not opened at autopsy.

Two-hundred forty-one patients received 60 mg. plus fever, and in this series there was one death, believed to be due to tuberculous meningitis. No postmortem examination was performed. This type of treatment was presently abandoned because of the high rate of clinical and serologic relapse—21.6 per cent.

The dosage of mapharsen was then gradually raised, and 488 patients have now received fever plus 1.76 mg. of mapharsen per kilo. Eleven of this series, or 2.25 per cent have been re-treated because of clinical or serologic relapse.

Of all the cases, 65, or approximately 7 per cent, did not receive the full amount of fever because of lack of cooperation, or due to the usual complications of fever therapy.

Of this series, 222 or 23.8 per cent have become sero-negative, and the serologic titer of 242 is declining. Unhappily, the statistical data given are so poorly arranged and the groups of cases so ill-defined that it is impossible to arrive at any conclusion regarding the 488 patients who have received what the authors estimate to be the optimum type of treatment.

Nathaniel Jones of the U. S. Public Health Service, working in conjunction with Warren, has been engaged in one-day treatment at Jacksonville, Florida. Patients at this facility receive five hours of fever at 105° F., with a single dose of 120 mg. of mapharsen at the close of fever. In respect to this, it is interesting to note that in Jones' cases, the persons who received mapharsen during or before fever had a high incidence of gastrointestinal and other reactions. At present, no data have been published from this source, but results are said to be promising.

What the future holds for the one-day treatment of syphilis no one can now pre-

dict. It is possible that this method may afford, in its present form or some modification, the Therapia Sterilisans Magna which is the ultimate goal of all syphilologists. It may well be that the answer is not yet. Only time, work, and the scientific method will allow its evaluation.

REFERENCES

1. Bessemans, A.: New experimental data on artificial hyperthermia, Ann. Med., 11:1933, 1938.
2. Bessemans, A.: Experimental contribution to study of antisyphilitic hyperthermy produced by physical agents, Am. J. Syph., Gonor. & Ven. Dis., 22:478, 1938.
3. Carpenter, C. M., Boak, R. A., and Warren, S. L.: The thermal death time of the gonococcus at fever temperatures, Am. J. Syph., Gon. & Ven. Dis., 22:279, 1938.
4. Epstein, N. N., and Cohen, M.: Effects of hyperpyrexia produced by radiant heat in early syphilis, with description of simple method of producing hyperpyrexia, J. A. M. A., 104:883, 1935.
5. Simpson, W. M., Kendell, H. W., and Rose, D. L.: The treatment of syphilis with artificial fever, combined with chemotherapy, Supplement 16, Ven. Dis. Information.
6. Bundesen, H. N., Bauer, T. J., and Kendell, H. W.: Intensive treatment of gonorrhea and syphilis; organization, objectives, activities and accomplishments of Chicago Intensive Treatment Center; preliminary report, J. A. M. A., 123:816, 1943.

THE PRESENT STATUS OF THE FIVE DAY INTENSIVE TREATMENT OF SYPHILIS

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The intensive treatment of syphilis, no longer an experiment but now a definite therapeutic technic, has shaped itself into two programs: a short, supervised method of intensive treatment which includes the various technics requiring hospitalization and close supervision during the treatment, and a longer ambulant method in which a tri-weekly dosage of mapharsen is given over a period of eight to ten weeks. The one day type of supervised intensive treatment is to be discussed in a separate paper this evening, and the ambulatory method of intensive treatment, sometimes known as the Eagle treatment, will also be discussed separately.

This paper deals with the five day principle of supervised intensive treatment, into which must be grouped all of the other intensive methods of therapy not included in the other two papers. These methods embody relatively the same general principles, although they may differ in the actual technic of administration.

It is conceded that in the intensive treatment of syphilis by any method, it is necessary to administer at least 1,200 mg. of mapharsen within the given treatment. Eagle has shown that the shorter the treatment period, the lower the dosage of mapharsen necessary, and the longer the treatment period, the greater the dosage of mapharsen, within a range of 1200 mg. to 1800 mg. It is also recognized that the efficacy of intensive treatment by any method is greatly enhanced by the addition of bismuth. Differences in treatment, therefore, depend not upon the dosage or the drug used, but upon the method selected for its administration and the convenience and safety of that method.

At the present time, the short form of intensive treatment, aside from the one-day treatment, to be alluded to here as the five day treatment, includes four separate technics. First, there is the slow continuous drip technic as described by the New York group, consisting of the administration of 240 mg. of mapharsen daily for five days, each daily dose being in 2,400 c. c. of 5 per cent glucose and given at the rate of 20 mg. per hour for 12 hours.

Second, a rapid drip modification has been developed in Detroit which consists of the administration of 1.2 mg. of mapharsen per pound of body weight, up to a maximum dose of 180 mg. dissolved in 1,000 c. c. of 5 per cent glucose solution administered intravenously in 60-75 minutes and repeated daily for five days. The total dosage by this method will be observed to be considerably less than the standard of 1,200 mg., amounting actually to 750-900 mg.

A third method of intensive treatment is the multiple injection method which consists of giving 60 to 100 mg. of mapharsen dissolved in 10 c. c. of distilled water once or twice daily and repeating this dosage daily until a total of 1,200 mg. has been given. This treatment lasts from six to 12 days, depending upon the dosage and the number of injections which may be given daily.

The Miami Valley Hospital group in Day-

ton, Ohio, has added fever therapy to the multiple syringe method with the duration of the treatment varying from ten to twenty days.

It is not the purpose of this paper to discuss the technic of these different methods in any detail. Some discussion of the individual comparative treatment results should be made, however. There is not sufficient evidence in the literature regarding the combination of multiple syringe technics with fever therapy to evaluate it adequately and I have had no personal experience with it. Since the multiple syringe treatment has been shown to have a rather higher incidence of complications than other means of intensive treatment therapy, we have not considered its use indicated in combination with fever therapy, although facilities for that method have been available at the Marine Hospital. The fact that fever therapy unquestionably increases the therapeutic efficiency of some drugs, including mapharsen, would indicate that if this combination does not also produce a higher number of toxic reactions, it might be a desirable method. Reports on the multiple syringe technic indicate that the incidence of reactions is at least as high, and probably higher, than with the slow drip administration as used by the New York group.

The rapid drip method as used by the Detroit group and the slow continuous drip are the two acceptable methods of short intensive administration which we can seriously consider. A comparison of the two methods shows that the rapid drip, because of its lower total dosage, had less reactions. The expected failure rate by the treatment for all kinds of syphilis was 18.3 per cent against the expected failure rate by the slow continuous drip of 13.9 per cent. The chief difference in the two failure rates lay in secondary syphilis, in which the rapid drip showed an expected failure rate of 27 per cent against a failure rate of 17.4 per cent with the slow drip. Primary syphilis also showed a higher failure rate. The relatively short series of cases presented by the proponents of the rapid drip method makes their low incidence of serious complications open to some question, since one or two cases would change their figures appreciably. Actually, there is not a great deal of difference between the two methods of treatment, except in the results of secondary syphilis, in which the beneficial effects of the higher dosage by the slow drip are notable.

Sixteen hundred patients receiving one of the two five day drip methods of treatment were reviewed by Elliott and his associates in June, 1941. The following essential facts should be emphasized from the large amount of statistical data presented.

The reactions to treatment: five treatment deaths were reported in the series, or .3 per cent. That is, one patient in 320 cases died as a result of the treatment. Death was due to hemorrhagic encephalitis from the clinical picture. Autopsy on three of the cases showed those changes consistent with cerebral anoxia, but failed to confirm the impression of hemorrhagic encephalitis or to reveal any definite findings which would permit a pathologic diagnosis.

The most common complaints and reactions in order of their frequency were: nausea, 60 per cent; primary fever, 48 per cent; secondary fever, 41 per cent; pain in arm, 41 per cent; cerebral symptoms (mainly headache), 31 per cent; toxicodermas, 11 per cent.

There was an extremely low incidence of renal and liver irritation or impairment of function, and of peripheral neuritis. Only two cases of clinical jaundice were seen in the series of 1,600 cases. The peripheral neuritis was transient and mild. There was complete absence of exfoliative dermatitis, blood dyscrasias and nitratoid reactions.

A great deal of emphasis has been placed upon deaths due to this form of treatment without recognizing the fact that a careful analysis of large series of cases has shown that deaths occur from the standard method of treating patients for a year to 18 months far more frequently than realized. Cole reported approximately one death in 300 completely treated patients. Other similar reports have appeared. It is notable

that unpublished information in some of the treatment centers now using the slow intravenous drip method has shown that some series of cases as high as 500 have been run without fatalities. It is believed that this is due to more experience in observing the premonitory signs which herald a development of such complications and that under careful supervision the death rate can be kept extremely low. There is no question but that the incidence of toxic encephalitis is higher with this method of treatment, but with experienced supervision the dangers of these complications can be eliminated. In our series of 57 cases at the Marine Hospital one man developed encephalitis with five convulsions, and with recovery in three days. Serious cerebral symptoms developed in one other patient, but the treatment was discontinued and he developed no convulsions and recovered uneventfully. The percentage of other toxic reactions was approximately the same as in Elliott's series. There were no cases of jaundice, one patient developed mild intercurrent pneumonia on the third day, but completed his treatment while receiving treatment for pneumonia. We found that with careful supervision the treatment could be given to almost all patients, with primary, secondary and early latent syphilis, and that serious reactions requiring discontinuance could be expected in about 2-4 per cent of the patients treated. It is my personal impression that to a great extent whether or not these serious reactions terminate fatally depends upon the amount of supervision the treatments receive. Our only reason for discontinuing this method of therapy was shortage of hospital personnel adequately to supervise the treatments.

The percentage of failures is 13 to 18 per cent in all patients treated. The serologic reversal in patients treated in this way may not take place for six months after the termination of the treatment. Therefore all patients must be closely followed in order to be pronounced cured.

The greatest value of intensive treatment lies in the number of patients who can receive adequate treatment. Some method of case follow-up and case holding is necessary in both intensive and routine antisyphilitic treatment. The follow up in the intensive cases is on *adequately treated patients,* while the follow up in the standard method of treatment is a method of case holding to keep the patient coming back to the clinic for a year and a half. The number of lost patients in the average treatment clinic using the standard method ranges from 40 to 75 per cent, in spite of the most elaborately organized and expensive follow up methods, complete with police enforcement and all the furnishings of an extensive epidemiologic routine. This means that adequate treatment is furnished to only 25 to 60 per cent of clinic patients, depending on the efficacy of the follow-up method. Relatively the same percentage of cures is obtained by the standard treatment method in the small number of patients adequately treated. By the use of the five day treatment it is possible to treat approximately 100 per cent of the patients diagnosed and to assure cures to 85 per cent of the patients treated. Subsequent treatment improves the prognosis in the resistant cases. The argument that this treatment is expensive and requires elaborate hospitalization facilities is not valid, in view of the cumbersome social service and case worker follow-up method frequently backed up by police enforcement which is necessary in order to effect adequate treatment to half the number of patients by standard methods. In dealing with a disease presenting the morbidity and mortality characterized by syphilis, a death rate of one in 320, or probably much less, should not deter the physician from assuring his patients and society the maximum of protection, particularly when it is apparent that experience and trained supervision can reduce this death rate materially.

It should be emphasized that there is no controversy between the short form of intensive therapy as embodied in the five day method and the Eagle treatment consisting of tri-weekly injections. Surveys of large series of patients indicate that the percentage of results is essentially the same.

It is without question that serious reactions are somewhat less by the longer form of intensive treatment.

The choice of treatment depends on the factors of social economics, exigency, and case holding. If the clinic population is transient or case holding methods are not satisfactory or difficult to enforce because of the improvident and unreliable character of the clinic population, then the shorter form of intensive therapy is desirable. When the questions of housing and care for eight to ten weeks are not significant or the type of patient is such that case holding for eight to ten weeks can approach 100 per cent, then the longer form of intensive treatment is preferable. In private practice, the longer intensive treatment is obviously most satisfactory.

THE TREATMENT OF EARLY SYPHILIS BY MEANS OF EIGHT WEEKS' MAPHARSEN THERAPY WITH BISMUTH

EXPERIMENTAL BACKGROUND AND APPLICATION IN PRACTICE

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Dr. Harry Eagle is responsible for the experimental work on which the tri-weekly schedule for mapharsen was based. Following the publication of reports on extremely short schedules for treating syphilis in man with massive arsenotherapy, it seemed important to find out on experimental animals the tolerance to certain schedules of treatment and the curative effect of such schedules on animals infected with syphilis.

Chinchilla rabbits were chosen for the experimental work, weighing 2.1 to 2.9 kg. and four to six months old. Two strains were used.

It was found that with respect to excretion, 50 per cent of the sublethal (or maximum tolerated dose) was excreted in 48 hours; over 65 per cent was excreted in seven days. The following figures show the findings with respect to tolerance of mapharsen:

10 mg. per kilo once weekly—tolerated.

10 mg. per kilo three times weekly—all died.

8 mg. per kilo three times weekly—tolerated six weeks.

Then 6.5 mg. per kilo three times weekly—tolerated six weeks.

It was found that the total amount could be increased by prolongation of a treatment schedule, but succeeding tolerated doses were smaller.

With respect to daily injections, the following data were obtained with respect to maximum tolerated dose:

4 mg. daily per kilo—four weeks.

5 mg. daily per kilo—two weeks.

4 mg. per kilo four times daily—one day.

2.4 mg. per kilo four times daily—four days.

These figures boiled down to this:

Daily injections permitted in four days, 31 mg. per kilo, while daily injections for a period of two weeks permitted only 65 mg. (compare with 10 mg. at one single dose).

It will be noted that 2.4 mg. four times daily for four days would amount to 38.4 mg. per kilo, at an average of one-quarter amount each time compared with the single tolerated dose of 10 mg. per kilo. Other investigators have determined that the tolerated dose per kilo for dogs was about the same as for rabbits. Man presumably is somewhat similar in this respect. (It should be borne in mind that the maximum tolerated dose killed no more than five per cent of the experimental animals—hardly a safe margin for human consumption.)

It was found that the maximum tolerated dose for continuous intravenous drip was 19 mg. per kilo compared with 10 mg. for a single intravenous dose. Repeated for four days it allowed a total of 45 mg. per kilo compared with the four doses daily for a total of 38.4 mg. per kilo. It is figured that the cumulative toxicity probably is somewhat counterbalanced by continued excretion.

The curative dose was determined by transfer of lymph nodes of infected rabbits

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six months after treatment. The following is the total curative doses on various schedules:

6.3 mg. per kilo for a single injection.

8.1 mg. per kilo for six weekly injections (six weeks).

7.7 mg. per kilo for 12 tri-weekly injections (four weeks).

As to daily injections:

6.1—3.0—6.4 mg. per kilo for one, four, 12 days, respectively.

5.9—6.2—3.6 mg. per kilo for one, two, four days respectively for multiple injections.

8.9—6.8—11.2 mg. per kilo for one, two, four days respectively, with intravenous drip.

Excluding the rather freakish four-day daily dose and multiple dose, and the continuous drip, the amount varied only from 5.9 to 8.1 mg. per kilo in time from 10 seconds to six weeks!

The margin of safety is expressed as the ratio between the maximum tolerated dose and the minimum curative dose. On any schedule, any desired margin of safety could be arrived at by lengthening (or shortening) the schedule and accordingly adjusting the dosage. Theoretically if the doses are as long as a week apart, some treponemes would propagate.

Many different schemes could be worked out showing varying margins of safety.

The following table shows the margin of safety for some typical schedules:

TABLE 1.

DEGREE TO WHICH ANTISYPHILITIC TREATMENT CAN BE INTENSIFIED IN RABBITS WITHOUT AFFECTING THE MARGIN OF SAFETY

Desired margin of safety	Approximate amount of treatment which will give desired margin of safety for various schedules of treatment				
	Weekly injections	Tri-weekly injections	Daily injections	Injections repeated 4 times daily	Intravenous drip (6 hours daily)
10	8 weeks, 8x1.0 mg. per kg.	3 weeks, 9x0.8 mg. per kg.	2 weeks, 12x0.5 mg. per kg.	4 days, 16x0.24 mg. per kg.	17 days, 17x0.7 mg. per kg.
8	7 weeks, 7x1.2 mg. per kg.	16 days, 7x1.1 mg. per kg.	5 days, 5x0.8 mg. per kg.	3 days, 12x0.4 mg. per kg.	12 days, 12x1 mg. per kg.
6	5 weeks, 5x1.6 mg. per kg.	12 days, 5x1.5 mg. per kg.	3 days, 3x1.3 mg. per kg.	2 days, 8x0.6 mg. per kg.	8 days, 8x1.5 mg. per kg.
4	3 weeks, 3x2.5 mg. per kg.	8 days, 4x1.9 mg. per kg.	2 days, 2x2.4 mg. per kg.	1½ days, 6x1 mg. per kg.	4 days, 4x2.9 mg. per kg.
2	.....	.....	.....	.....	1 day, 1x9.0 mg. per kg.

COMMENT

1. In the various intensive schedules which have been used for the treatment of early syphilis in man, the dose of mapharsen which has "cured" a satisfactory proportion of patients has been largely independent of the frequency of injection or the duration of treatment. This curative dose has been 20 to 30 mg. per kg., or approximately 1,500 mg. in a man weighing 60 kg.

2. The margin of safety provided by any intensive procedure is therefore primarily a function of its toxicity. That margin of safety, calculated from the animal data on toxicity, has varied from three to 10 in the treatment schedules which have been used in man. The observed incidence of toxic reactions and of deaths has been in complete accord with, and predictable from, this calculated margin. Thus, the administration of 1,200 mg. in a five-day intravenous drip, with a safety factor of 3.0, has resulted in a mortality of 1:200, and serious toxic reactions in one in every 100 patients treated. Standard weekly practice, with a safety factor of 10, has a mortality of less than 1:3,000; and treatment schedules with intermediate factors of safety have resulted in a correspondingly intermediate incidence of toxic reactions and deaths.

3. It is estimated that a margin of safety of six to eight is necessary to reduce the mortality of antisyphilitic treatment to less than 1:1,000. With the drugs and methods now available, no treatment schedule completed in 20 days or less meets that reasonable requirement, no matter how the injections are given. That margin of safety would, however, be provided by giving the

total curative dose in tri-weekly injections for seven weeks, daily injections for approximately six weeks, or multiple daily injections, or an intravenous drip for an estimated period of four to six weeks.

4. The tri-weekly schedule has the important advantage of permitting treatment to be carried out on an ambulant basis in the average clinic. This method is now under study in 80 cooperating clinics. The size of the individual dose has been fixed at approximately 1 mg. per kg., with a maximum of 80 mg. and a minimum of 40 mg. The duration of treatment has been varied from six to 12 weeks. The minimum effective total dosage, the advisability of giving concurrent injections of bismuth, and the applicability of the procedure to the treatment of latent syphilis are some of the factors which have been considered. Subsequently it was found that over the cooperative clinics as a whole, patients receiving only mapharsen had 12 per cent failures compared with 1.5 per cent in those who had mapharsen and bismuth. This includes all types of early syphilis and considers all types of failures such as relapses, serolapses, and persistent positives.

In the New Orleans Clinic we used approximately 1 mg. per kilo per dose for 24 doses given three times weekly for eight weeks. The dose varied from 40 to 80 mg., depending on weight. Eight injections of bismuth subsalicylate, 0.2 gm. each, were given concurrently, being given at every third injection of mapharsen. This schedule of treatment has been used since March, 1942. The data given do not include all who have been accepted for treatment or all who have finished. They do include all patients taken consecutively who finished or should have finished treatment by June 1, 1943. Naturally the figures on observation of these cases has continued and is up to date as of February 1, 1944.

Table 2 shows the color and sex distribution of patients, and is self-explanatory:

TABLE 2.

	Male	Female	Total
White	17	15	32
Colored	77	51	128
Total	94	66	160

Table 3 shows the diagnosis and the distribution according to sex:

TABLE 3.

	Male	Female	Total
Primary	52	12	64
Secondary	36	52	88
Infectious Relapse	6	2	8
Total	94	66	160

All of these patients had positive dark field examinations.

It is noted that the males with primaries outnumbered the females 52 to 12, whereas the females with secondaries outnumbered the males 52 to 36. No doubt this is what one would expect, since the females would quite likely overlook the primaries. It may not be significant, but one can speculate that having overlooked the primaries, the females would go to secondaries before being recognized more often than would males, as witness the greater number of females with secondaries in this series. There were six males and two females with relapses when admitted. Could this greater number in the male be due to the probability that less men than women have already had secondaries before treatment was begun originally?

Table 4 shows the number in each sex who finished treatment, and the percentage of each:

TABLE 4.

Number who began Treatment			Number who finished treatment					
Male	Female	Total	Male	Per cent	Female	Per cent	Total	Per cent
94	66	160	56	59.57	49	74.24	105	65.62

It should be mentioned that seven males were inducted into the Army, and therefore could not be expected to count at all in the series showing what should normally be expected of their attendance. As a rule, such inductions were done before we were notified by the patients that they were pending. This does not mean that no further treatment was done. It merely means that we could not be further responsible for the schedule. It will be noted that 49 of the 66 females, or 74.24 per cent, finished; whereas only 56 of the 94 males (59.57 per cent) finished. Eliminating the inductees

(a condition peculiar to males only) one would have 56 of 87 finishing, or 64.36 per cent.

Table 5 shows the time required for the patient to finish the *prescribed eight weeks'* treatment:

TABLE 5.

	Male	Per cent	Female	Per cent	Total	Per cent
8 weeks	18	32.14	19	38.78	37	35.23
9–16 weeks	30	53.57	25	51.02	55	52.38
17+weeks ..	(8	14.29	5	10.20	13	12.38)
Total	56	100.00	49	100.00	105	100.00

It has been arbitrarily divided into three classifications. While there is no exact way of evaluating the efficacy of treatment stretched out over as much as twice the desired time, it seems that the results might reasonably approach the approved eight weeks' schedule and it would seem that treatment requiring over sixteen weeks is not sufficiently accelerated to be called intensive treatment.

It will be noted that of the 56 males who received 24 mapharsen and eight bismuth injections, 32.14 per cent finished in the eight week's time; of the 49 female patients who finished treatment, 38.78 per cent did so in the prescribed time. Combining the sexes, 35.23 per cent finished in eight weeks. Of the males, 53.57 per cent, and of the females, 51.02 per cent finished treatment from nine to 16 weeks inclusive. A total of 55 males and females finished in the nine to 16 week group, representing 52.38 per cent of those who finished. Combining the two foregoing groups, 92 patients finished treatment within a reasonably intensive schedule, representing 87.62 per cent of those who finished and 57.50 per cent of all those who began treatment.

Of the 55 who never finished treatment, 20 had less than 7 doses of mapharsen; 18 had from seven to 12 doses; 16 had from 13 to 18 doses; and one had from 19 to 23 doses.

Of the 48 males who completed treatment in 16 weeks or less and who had positive Kahns at the beginning, varying from four to 400, 23 had a reduction at the end of treatment and 22 had negative Kahns at the end. Of the 44 females who finished and who had been positive, 26 had a reduction in titre and 17 had negatives. The titres were essentially similar at the beginning, so far as was noted. Fifteen of the 22 males who had a reduction in titre at the end had further reduction during observation (four were not followed further). Twelve of the 20 females with a reduction in titre had still further reduction during observation, (three not followed). One male relapsed (had a recurrence), 1.9 per cent. His lesion was negative on darkfield examination, but his Kahn titre rose to 40 at the time. Originally his diagnosis had been seronegative primary. He had had three negative bloods and a negative lumbar puncture during the period of observation. There were two infectious relapses, 4.5 per cent (in females) both with positive darkfields and increased Kahn titres. One had had no follow-up, the other had ended treatment with a quantitative Kahn of 4, subsequently it was negative. They could have been considered either reinfections or relapses. The diagnosis had been secondary syphilis in each case, primarily. The elapsed time since cessation of treatment was seven and 11 months, respectively. One had an ulcer of the cervix, the other mucous patches of the vagina, as "recurrences." There were two each with serolapses only, in each sex. There was one of each with no reduction in titre throughout treatment or observation. Two males who finished treatment were seronegative throughout treatment and observation.

Table 6 shows the per cent of patients who had reactions, and some who we judge could not be further treated with such therapy:

TABLE 6.

	Male	Reaction per cent	Female	Reaction per cent	Total	Reaction total per cent
Mild reaction	7	7.44	15	22.73	22	13.75
Severe reaction	1	1.07	14	21.2	15	9.37
Stopped because of reaction*	1	1.07	6	9.09	7	4.37

*Reactions based on the total number of patients placed on this treatment, and not on the number who completed it.

Of this group, 4 females finished treatment with moderate decrease in dosage of mapharsen.

Table 7 shows the distribution of patients who finished despite reactions:

TABLE 7.

	Male	Female	Total
Finished treatment with:			
Mild reaction	4	14	18
Severe reactions	0	4	4

The mild reactions were as follows:

For the males: Three, nausea (one also had bleeding gums); four, nausea and vomiting.

For the females: Six, nausea (one with diarrhea); four, nausea and vomiting; two, chills and fever; one, pain in legs; one, retinitis with brick-dust opacities of vitreous of the right eye with failing vision. History of previous eye complaint of similar nature. Ophthalmologist thought not due to syphilis nor to treatment; one, diarrhea and edema of ankles.

Of the severe reactions: One male with icterus, chills and fever; eight females with severe nausea and vomiting (one with chills); three with icterus; one with blood dyscrasia, R. B. C. 2.5 million, W. B. C. 2200 following fever and moderate shock. Marked icterus, later; one with nausea and vomiting, later tolerated neosalvarsan.

Most of the reactions of any consequence occurred during the second and third week (fourth to tenth dose).

There were no deaths.

The follow-up (observation) of the 76 patients who finished treatment, and who were observed later, was as follows:

7 followed for 1 month
8 followed for 2 months
9 followed for 4 months
6 followed for 5 months
5 followed for 6 months
6 followed for 7 months
5 followed for 8 months
8 followed for 9 months
4 followed for 10 months
3 followed for 11 months
1 each followed for 12, 13, 14, and 17 months.

On an average, the 76 patients followed were observed for almost six months. Sixteen were not observed after finishing treatment.

Thirty-one patients had lumbar punctures during observation. All were negative. These lumbar punctures are scheduled at the third month in order to get them while the patients are still available, if possible. Some were done as late as nine months.

SUMMARY

There were no deaths among the 92 patients out of 160 who began intensive (Eagle) schedule fixed at approximately 1 mg. per kilo three times weekly, but extended in time (not amount) by 55 of them to as much as nine to 16 weeks inclusive. The period of observation following treatment averaged approximately six months. Spinal fluids were negative on the 31 examined. Two females had infectious relapses (unless one should consider them reinfections). One male had a clinical relapse not proved by darkfield. There were two with serorelapses only, one of each sex. Altogether, seven of the 92, or 7.6 per cent could be considered treatment failures with the schedule indicated, considering the fixed positives, the serolapses, and the probable infectious relapses. If the three recurrences should be considered as reinfections or unproved relapse, as the case may be, there still would be four treatment failures, or 4.35 per cent.

REFERENCES

1. Eagle, H., and Hogan, R. B.: An experimental evaluation of intensive methods for the treatment of early syphilis. I. Toxicity and excretion, Ven. Dis. Inform., 24:33, 1943.

2. Eagle, H., and Hogan, R. B.: An experimental evaluation of intensive methods for the treatment of early syphilis. II. Therapeutic efficacy and margin of safety, Ven. Dis. Inform., 24:69, 1943.

3. Eagle, H., and Hogan, R. B.: An experimental evaluation of intensive methods for the treatment of early syphilis. III. Clinical implications, Ven. Dis. Inform., 24:159, 1943.

DISCUSSION

Dr. M. T. Van Studdiford (New Orleans): I think such timely discussions as the papers of Drs. Billings, Knight, and Agee call for praise because of their conservatism at a time when so many read the Reader's Digest "One Day Cure."

In considering a standpoint for treatment we must consider the objectives: Public Health Agencies wish to stop the spread of syphilis—that is kill the family tree while it is a chancre now.

The Army, Navy and maritime agencies want to put man-power back at work; the private practitioner wishes to cure his patients as quickly as it can be safely done.

Dr. Politzer, years ago, tried multiple injections with neosalvarsan but reactions were too frequent. So years passed before his group began to use the less toxic arsenoxide. When one thinks of the arsenicals in a comparative way, old salvarsan "606" would compare to 100 proof straight whisky; neosalvarsan to 90 proof whisky in a highball, and mapharsen, phenarsine or any of the other arsenoxides as Scotch whisky highballs. We see that the strongest gives the biggest headache and so forth. All have their places in therapy but must be used knowingly. If one treats syphilis in its early stages and with a rapid method it has been shown here that a total of 1200 to 1400 mg. of arsenoxide should be administered. This can be done with the Schoch-Alexander seven day method, the modified Eagle-Hogan method for eight weeks, or the fever-arsenoxide one day method.

All can be given in most instances, so few patients in each series have been treated that one or two deaths or a few reactions cause large changes in the percentages but as more and more series are added from other clinics we can then be able to evaluate results and arrive at a quicker, safe method more up to date. Probably the twice a week arsenical and one bismuth injection for the ambulatory worker or the three a week arsenical and one bismuth injection for the hospitalized patient appears to me to be safe, conservative yet fast enough to cover the desires of all groups. I think the above papers tend to bear out the opinion that we have gone a long way in our advances in therapy.

Dr. V. Medd Henington (New Orleans): The papers that have been presented tonight have covered the subject of "Intensive Treatment of Syphilis" so well that there is little room for discussion. However, there are a few points I would like to bring up for your consideration: First, we must remember and always be conscious of the fact that the drugs used in syphilis are of such a character that to treat the disease effectively makes a certain minimum risk inevitable. We must also remember that it is not always possible to apply animal experimentation directly to clinical usage, for experimental animals do not develop optic atrophy, exfoliative dermatitis, or toxic hepatitis, which are among the most serious reactions observed in human subjects.

The rapid or intensive treatment of syphilis is not something that has sprung up in the past few years, although it was as we might say popularized by Chargin, Hyman and others in 1934. For the rapid treatment of syphilis is as old as the arsphenamines for was it not Ehrlich's dream to cure the disease with one injection or, as he called it, the magic bullet.

As early as 1910 Hoffmann attempted a three day cure of syphilis by the daily simultaneous intravenous and intramuscular administration of arsphenamine.

Mapharsen, too, is not new in the treatment of syphilis for it was first discovered by Ehrlich who discarded it because of its supposed toxicity. However, more recently it was revived by Tatum and Cooper. Mapharsen has gained much popularity in the past few years for since the action of the arsphenamine is now rather definitely proved to be due to the formation of arsenoxide in the body, it is only logical to believe that direct administration of arsenoxide would have definite advantages. Since only part of the arsphenamine injected is converted into arsenoxide in the body, the balance must be excreted in the form of various arsenical compounds. This excess arsenic may be one of the causes of untoward reactions. We know that arsphenamine "606" is excreted primarily in the feces and that neoarsphenamine is excreted primarily in the urine. I am not familiar with the primary route of excretion of mapharsen and perhaps this is one question that can be answered later in the discussion by Dr. Agee.

I noticed that Dr. Agee makes the statement that no treatment schedule completed in 20 days or less meets the safety factor of 10 or in other words a mortality factor of less than 1-3000.

If I may be allowed to bring personal experience into the discussion I should like to tell you about some of the work that is now being done at Columbia University. At Columbia we treated only male patients simply because we were allotted only one ward in which to carry out our experiment. All patients presented either primary or secondary lesions with a positive darkfield. These men were given the original "606", which is commonly known as old arsphenamine. One group was given four injections daily for six days, making a total of 3.6 gm. The other group was given 1 gm. in one intravenous injection every other day for three days, making a total of 3 gm. The youngest patient was 15 and the oldest 53 years. There was not one fatality in 300 cases. Nausea, vomiting, and transient neuritis were the worst reactions; there were no cases of exfoliative dermatitis, liver necrosis or the dreaded hemorrhagic encephalitis. It was our impression that the frequency of injections and not the total amount of arsphenamine was important in producing toxic reactions. For the patients who received only 3 gm. of arsphenamine had but three intravenous injections while the patients who received 3.6 gm. had a total of 24 injections. Yet the patients receiving only three injections had many more reactions than those patients receiving 24 injections and 0.6 gm. more arsphenamine. It was also interesting to note that every patient who came in with pri-

mary or secondary syphilis had a strongly positive Ehrlich's test for urobilinogen in the urine and practically every patient had a 4 plus cephalin flocculation. It is further interesting to note that both of these tests became negative within 24 to 48 hours after treatment was begun.

The eight week treatment as presented tonight was reported to have a 7.6 per cent failure in 92 cases. Although we must realize that 92 patients comprise a rather small group I think that the percentage of failures is very small for, with the regular 18 month anti-luetic treatment the percentage of failure is around 10 per cent.

In conclusion, we can say that the massive therapy of syphilis is still in the experimental stage in the sense that it is still too soon to determine the end results of treatment, as well as all the dangers of the method, which obviously are greater than those of standard methods of treatment.

As Goldblatt once said, "Syphilis waits twenty years to destroy our therapeutic illusions."

BUY

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THE DOCTOR FIGHTS

On Tuesday evening over the Columbia Broadcasting Network there is to be heard a radio program which should be of great interest to all physicians. The program that was heard just prior to writing this editorial was one of the best that we have heard for a long time. It was dramatic, it was well sustained, and the actors were vocally splendid. It might well be that some casual critics will complain that the doctor was almost deified in this program. To a large extent physicians in general were held to be professional people of great unselfishness, marked generosity and unfailingly courageous, but elsewhere, in various non-medical publications and in critical circles, the doctor is often freely criticized. Even if this program does possibly put the doctor on a higher plane than he as an individual thinks he belongs, nevertheless, it is pleasant and nice to hear agreeable things spoken about the most unselfish and selfless profession in the world which is often unjustifiably censored.

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THE DISTRIBUTION OF PHYSICIANS IN SOUTHEASTERN STATES

A. M. Lassek*, head of the Department of Anatomy of the Medical College of the State of South Carolina, has prepared a statistical report on the distribution of physicians in Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, North and South Carolina and Virginia. This is a most detailed study which will be buried in a journal of very small circulation so it might be worth while to point out some of the facts that Dr. Lassek has obtained from his survey.

The ratio of resident physicians to the population in the above states is 1:1080, which is a lower ratio of doctors to the population than any other section of the country. Alabama has one doctor for every 1,334 persons in the state. Other states have a somewhat lower ratio and only Louisiana, Tennessee and Virginia, of the Southern states, have ratios under 1:1000. In seven of the states there are at present thirteen medical schools on a four-year basis and three two-year schools. In 1942 there were slightly over 28,000 physicians who graduated from Southern schools or, expressed in another way, 15.8 per cent of all the registered doctors in the United States. Thirty-eight per cent of the doctors remained within the state in which the medical school from which they graduated was located. Twenty-six per cent located in other Southern states,

*Lassek, A. M.: The role of the Southeastern schools of medicine in the national distribution of physicians, J. Assn. Am. Med. Colleges, 19:217, 1944.

whereas 35 per cent engaged in the practice of medicine in states not located in this region. In all, 62 per cent of the graduates of one or another of the Southern schools did not remain in the state where the school was located.

Tulane, of all the Southern schools, has the greatest number of living graduates, 3,481 physicians scattered all over the country. Of these several thousand graduates, approximately one-third remained to practice in Louisiana, one-third in Southern states and one-third elsewhere in this country. Louisiana State University has not graduated many students as yet. Nearly three-fifths of their graduates have remained in Louisiana, practically 28 per cent have moved away from the Southeastern states.

Graduates from schools from the North, East and West have immigrated to the South. There are 7,725 doctors who have moved to the Southeastern states. If the graduates of Southern schools had not moved out of the South, and to this group were added the group from the North, the ration of physicians to patients would be 1:721.

Distribution of doctors in the Southeast is considered to be unfavorable and the reason for this may be attributed properly to per capita income which is considerably lower than any other of the six regional subdivisions of the United States. The rural population of Louisiana, for example, does not have a sufficient number of doctors per patient in spite of the fact that in this state the ratio is much better than it is in most of the other Southern states. New Orleans, on the other hand, has a very pronounced lowering of physicians to patients ratio. In this city there is one doctor to every 417 persons. These figures are somewhat higher than in other large cities in the South. Little Rock, for example, has one doctor to every 368 persons; Columbia, S. C., 1:260. In some of the states in rural areas the doctor-patient ratio is 1:2500. In some of the very poor counties of the South the ratio is as high as 1:5000. Definitely the urban population of the South is well supplied with doctors, the rural areas poorly supplied. Lassek points out that legislators have the misguided opinion that if a man graduates from a state university he will settle in that state and that the distribution of physicians throughout the state would be such that all urban, suburban and rural areas would be well taken care of. This is absolutely incorrect as Lassek points out. Furthermore, the state that has the best regional distribution, Florida, has no medical school. It is amply supplied with doctors, probably because Florida has the largest income per capita of any of the Southern states.

STUDIES OF HUMAN PLASMA

The entire July issue of the Journal of Clinical Investigation (vol. 23, July 1944) is devoted to chemical, clinical and immunologic studies on the products of human plasma fractionation. These studies were conducted by a group of scientists at various laboratories throughout the country under contract, recommended by the National Research Council's Committee on Medical Research, between the Office of Scientific Research and Development and the particular University laboratory. They represent a conjoint investigation which is almost unparalleled in the history of scientific research.

Many of the studies are of particular interest to the physiologist, biochemist or the immunologist and for the most part have but little direct significance to the clinician, although the whole series taken together are fundamental in the understanding of plasma therapy and to the clinician should be of great value if he wishes to know the why and the wherefore of many of the practices carried out in the ordinary art of medicine. Of course in war surgery the information already obtained has been of extreme value to the casualty suffering from shock or the shock-hemorrhage syndrome.

A few of the distinctly clinical observations might be noted here. The use of dried albumin is an excellent example.

This fraction of the plasma may be extracted and dried. The amount that may be used as a temporary expedient represents an extremely small quantity which might be carried by any doctor in his emergency kit. A standard package of 25 grams of albumin diluted to 100 c.c. is equivalent in its osmotic effect to 500 c.c. of citrated plasma. There was found to occur prompt improvement after the injection of this concentrated albumin into a series of patients with shock and burns. It is not harmful. The package is compact and available for immediate and rapid administration. Furthermore it is stable and pyrogenic reactions do not occur. In patients who have a notable loss of serum albumin as in those with chronic hypoproteinemia for example, in nephrosis and in cirrhosis of the liver, the concentrated albumin may be of great service in the treatment of these patients. The albumin therapy increased arterial pressure and cardiac output in patients suffering from shock. For subsequent treatment where there has been a severe anemia whole blood should be given when available.

Normal human gamma globulin was studied as to its antibody content. It was found that this globulin did contain antibodies reacting to diphtheria toxin, streptococcal toxin, influenza A virus and mumps virus. These antibodies were concentrated from fifteen to thirty times when compared to pooled plasma. As a matter of fact the potency of fraction II, which is the fraction with which these papers are dealing, is approximately that of convalescent serum. As Enders says, the implications of these findings, in regard to fraction II as an agent in the prophylaxis and therapy of disease, are great.

Measles is a disease which, in the ordinary healthy child, is of no particular moment but in certain children convalescent serum has been used repeatedly to prevent or modify the course of the disease. Two groups of independent observers have found that fraction II definitely modifies the disease, makes it less severe and in several instances prevented the development of a rash, although Koplik spots were present. In children exposed to measles it prevented the development of the disease in 71 per cent of the cases, whereas amongst the controlled series 89 per cent developed measles of average severity.

Fibrin foam, in another series of studies, was found to be an excellent hemostatic agent, notably in the control of oozing in neurosurgery, and also in the prevention of adhesions between damaged nervous tissue and adjacent structures. Lastly, another group of investigators have shown that bovine serum gamma globulin is highly efficient in serum-protein regeneration.

The application of these studies, undertaken largely as result of war, to civilian needs is obvious. In the not too near future it is quite possible that human or bovine serum gamma albumin will play a most important part in the armamentarium of the physician who is treating disease or who is operating on patients. It can readily be foreseen that in human serum albumin there is an extremely potent therapeutic principle which will advance materially the satisfactory treatment of patients.

ORGANIZATION SECTION

The Executive Committee dedicates this page to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.

An informed profession should be a wise one.

EMERGENCY MATERNAL AND INFANT CARE PLAN

A great deal of water has run under the bridge in regard to the EMIC plan since the meeting of the House of Delegates of the State Society which was held in April of this year and it is the thought of the officers of the organization that it might be a good idea to acquaint our members with the present status of the plan as it has been

worked out in the state up to date. Immediately following the meeting of our House of Delegates our past president, Dr. C. C. deGravelles, made a trip to Washington for the purpose of presenting to the sub-committee on appropriations the brief on this subject prepared by a special committee and approved by the House of Delegates. This brief was published in the organization section in the June issue of our Journal. Dr. deGravelles reported that the committee was very courteous to him and stated that the manner in which the facts were presented far surpassed most of the major pleas made before them by other organizations and individual physicians and complimented him on the splendid presentation made by the doctors of Louisiana. As a whole the committee seemed to look favorably upon the ideas submitted in our brief, however the final action taken by the Government was to continue operation of the plan as it had been handled previously, increasing the financial assistance to carry out the plan, disregarding all objections raised by Louisiana physicians as well as other physicians throughout the country.

Attempts have recently been made to complete a survey of the operation of the plan in the State of Louisiana including number of deliveries made by physicians, indicating number handled under the EMIC plan. However, due to the fact that the Maternal Division of the State Health Department has not complied with repeated requests for such information, we are unable to present exact figures at this time.

The Executive Committee of the Orleans Parish Medical Society and the general membership of that society approved the action of the House of Delegates and requested Dr. David E. Brown, Director of the State Department of Health to do all he could to aid in the establishment of the principle of the allotment plan in the handling of these cases. A letter has been received from Dr. Brown in which he states: "I wish to assure you that I shall be glad to do everything that I can to further the resolution which was adopted at the last meeting of the House of Delegates of the Louisiana State Medical Society regarding the Emergency Maternal and Infant Care Program in this state. We agree with you that if this program was administered directly with the individual, much more time would be available for the personnel of our Maternal and Child Health Section to do generealized public health work. Therefore, we shall make every effort to have the allotment payment plan for the maternal and infant welfare program, as approved by the State Medical Society, put into effect."

Attention of the Committee on Maternal Welfare has been called to the fact that one of the state institutions has been taking care of some of the EMIC cases. It has been ruled by the Attorney General of the State of Illinois that these cases can not be handled in the State of Illinois by charitable state institutions. This ruling was based on the fact that the plan was established in order to give private care to these patients as they are not charity cases. The members of our Committee on Maternal Welfare were canvassed and it was found that it was the unanimous opinion of the committee that charity hospitals in this state should not participate in this plan for the same reason as stated in the decision of the Attorney General of the State of Illinois.

Representative Miller, of Nebraska, has introduced a bill (H. 4663) in Congress which approves the transfer of operation of the Emergency Maternal and Infant Care Plan from the Children's Bureau of the Labor Department to the Public Health Service. The reason for this suggested transfer is that the plan involves medical care and it is therefore felt that it should be handled and operated by a medical body and not by a Labor Board which is composed primarily of labor representatives and social agencies which are unanimously opposed to practically every suggestion offered by the medical representatives on the committee of the Labor Department. The members of our Committee on Maternal Welfare have approved the suggestion that we communicate with our representatives and senators in Washington asking that they approve this bill, endorsing the removal of

the plan from the Labor Department to the Public Health Department. It is suggested, therefore, that all members of our organization who are interested in this problem write their representatives asking that they take an active part in helping to have passed this proposed legislation.

The East Baton Rouge Parish Medical Society recently adopted the following resolution: "Whereas, The program now in operation for maternal and infant care for wives and infants of enlisted men in the four lower grades is unsatisfactory to the members of the East Baton Rouge Parish Medical Society and, in many instances, to the enlisted men and their families; and, Whereas, The Emergency Maternity and Infant Care Program is a definite form of bureaucratic medicine brought upon the profession as a war emergency measure during this period of stress; be it therefore Resolved, That the members of the East Baton Rouge Parish Medical Society withdraw from participation in the EMIC program and be it further Resolved, That, for the duration of the war, the members of the East Baton Rouge Parish Medical Society will render medical services, without remuneration, to the wives and infants of enlisted men in the four lower grades." This resolution indicates that the plan, as it is operated at present, is meeting lack of cooperation of the medical profession of the state due to the manner in which it is handled by the government. The fact that the members of the Baton Rouge Society will handle these cases without remuneration indicates that the medical men of the state are not looking at the question from a financial viewpoint and are willing to do their share without regard to personal interest. These patients will probably, in this way, be given better service than if they were handled under the present set-up of the EMIC plan.

Recently a questionnaire was sent to the entire membership of the Orleans Parish Medical Society to ascertain how many were interested in taking care of EMIC patients, requesting that the form be returned if the doctor wished to handle these cases. Out of a membership of more than five hundred only two responded that they would agree to cooperate in handling cases under this plan. This shows again how the medical profession of the State of Louisiana feels in regard to this matter.

In the most recent issue of the Western Journal of Surgery, Obstetrics and Gynecology an editorial appeared in which it was brought out that Miss Lenroot and her co-workers are taking entire credit for the operation of this plan and the service rendered and are giving no credit to the medical profession for the part they are playing in the operation of the plan. It is apparent, from such statements, that the medical profession is not being dealt with fairly by the Government; responsibility for the work being carried on placed on the doctors but credit given to non-medical groups, which is evidence of the fact that the plan is just another step in an attempt toward socialization of medicine which is being carried on by the bureaucrats in Washington without the altruistic motive of serving those in the armed forces of our Country.

The Maternal Welfare Committee has solicited the various Louisiana candidates, both opposed and unopposed, for election to the Congress of the United States, asking their reaction and opinion in regard to the Wagner - Murray - Dingell Bill, the Miller Bill, and also the bill regarding deferment of pre-medical students. All of the replies received have stated that these candidates are in favor of all bills which would benefit the medical profession and are opposed to those in conflict with the desires of the medical profession. Those who claimed they did not have sufficient knowledge to discuss these issues stated that they will be open to advice from those who know more about these matters than themselves by consultation with members of the medical society. The reaction of these men shows that if the medical men would state their

case to the men running for public office and get an expression from them before their election, nearly any honest public official will be most willing to cooperate with us in regard to medical matters when properly approached.

Edwin L. Zander, M. D., Chairman
Committee on Maternal Welfare

LOUISIANA STATE MEDICAL SOCIETY NEWS

CALENDAR

PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

NATCHITOCHES PARISH

A meeting for discussion of Senate Bill 1161 was held for the physicians of Natchitoches Parish in Natchitoches on the night of August 18. Principle speakers at this meeting were Dr. David E. Brown, Director of the Louisiana State Board of Health, Dr. Walter F. Couvillion, Councilor of the Eighth District and Dr. P. T. Talbot, Secretary of the State Society.

AN IMPORTANT SYMPOSIUM

A symposium on the Heart and Circulation will be held at the Louisiana State University, School of Medicine, 1542 Tulane Avenue, New Orleans 13, Louisiana on October 25-27, 1944, from 9:30 a. m. to 5:00 p. m. each day. Those who are interested are invited to attend. No fee is charged. The visiting participants are Dr. Visscher, University of Minnesota, who will discuss cardiac efficiency and metabolism; Dr. Isaac Starr, University of Pennsylvania, who will discuss the ballistocardiograph; and Dr. Frank N. Wilson, University of Michigan, who will speak on electrocardiography. Other speakers are from Tulane University and Louisiana State University.

BASE HOSPITAL NO. 24

The latest reports from private correspondence and from the *Times Picayune* indicate that Base Hospital No. 24 (Tulane Unit) has been recollected and is now functioning as a unit some 60 miles from Florence. The Unit has been assigned to a recently completed tuberculosis sanitarium built by Mussolini for his veterans. It is situated in the outskirts of a large town and "has all the comforts and conveniences afforded by Touro or Charity Hospital."

While some of the members of the Unit were stationed in Rome they had the rare privilege of having an audience with the Pope.

DR. C. L. WILLIAMS PROMOTED

Dr. C. L. Williams who has been medical director of the Southern district of the United States Public Health Service has been promoted to the rank of Assistant Surgeon General and will leave for Washington the first part of August. Dr. Williams has been in New Orleans since July, 1940. During this period of time he has come in contact with many members of the medical profession. He has been an outstanding help to the state and city boards of health and he has taken an active part in many of the civic organizations. The many friends of Dr. Williams will be glad to hear of his promotion but sorry to hear he is leaving New Orleans. In Washington he will be in charge of the Bureau of State Services.

Dr. Otis L. Anderson is scheduled to succeed Dr. Williams.

DOZIER HONORED

The many friends of Major Horace B. Dozier, who graduated from Tulane Medical School in 1939, will be pleased to hear that he has been decorated again; this time with the Legion of Merit Award.

OFFICE OF COLLECTOR OF INTERNAL REVENUE

By Public Law 414, 78th Congress, effective July 1, 1944—the substance "isonipecaine," commonly known as "demerol," and any substance identified chemically as 1-methyl-4-phenyl-piperidine-4-carboxylic acid ethyl ester, or any salt thereof, by

whatever trade name designated, have been brought under provision of the Federal narcotic laws. *No provision is made to exempt preparations in this category.*

Registration: All manufacturers, wholesale and retail dealers, and practitioners, procuring or prescribing "demerol" must be registered in appropriate class and must submit to Collector on or before September 1, 1944, on appropriate Form 810-E, 811-C, or 713, an inventory of all stock on hand July 1, 1944. Any of the above having registered and secured special tax narcotic stamp for fiscal year beginning July 1, 1944, will not be required to re-register for selling, dispensing, or prescribing "demerol" and its derivatives. However, if such narcotic preparations were held on July 1, 1944, and not included in the inventory filed, a supplemental inventory will have to be submitted, listing only stock of demerol and its derivatives on hand July 1, 1944.

All transactions involving "demerol, etc., must, therefore, be made pursuant to official narcotic order forms or prescriptions and must be reported in monthly narcotic returns in the same manner as opium, coca leaves, and their derivatives."

NEWS ITEMS

Lt. Col. Ambrose H. Storck addressed the annual meeting of the State Medical Association of Utah in Salt Lake City on August 25. Colonel Storck spoke on "Abdominal Wounds; Management and Results in the Present War."

Announcing that the American people had contributed an all-time record of $10,973,491 to the 1944 Fund-Raising Appeal of The National Foundation for Infantile Paralysis, Basil O'Connor, Foundation president, declared last night that these donations will permit an expansion of the war against the children's enemy on the home front.

With epidemics or serious outbreaks now taking their toll in twelve of the states of the nation, Mr. O'Connor pointed out that the number of cases reported is already higher than for the comparable period last year when the country suffered its third worst epidemic.

In the first 31 weeks of 1944, the United States has had more cases of infantile paralysis reported than at any comparable time shown on the records in 28 years, The National Foundation for Infantile Paralysis declared today.

Latest figures from the U. S. Public Health Service, showing state reports through August 5, reveal a total of 3,992 cases, the National Foundation said. This is 1,226 cases more than reported for the same period last year when the nation suffered its third worst polio epidemic, and 1,089 cases more than in 1931 when the second worst outbreak was recorded. The records of the worst outbreak in 1916 show there were 6,767 cases by August 1 of that year.

In five states where the outbreaks are in epidemic or near-epidemic proportions, the total cases reported through August 5, 1944, are higher than those states reported for the entire year of 1943. They are:

State	*Through Aug. 5, 1944*	*Entire year of 1943*
New York	902	692
North Carolina	470	37
Kentucky	377	157
Pennsylvania	284	143
Virginia	205	61

The serious or threatening outbreaks this summer are confined almost entirely to states east of the Mississippi, while last year's were largely west of the river.

THE DOCTOR FIGHTS

The dramatic development of surgery has reduced the death rate of war wounded in army and navy hospitals to 3 per cent against 8 per cent in World War I, Dr. Irvin Abell, chairman of the board of regents of the American College of Surgeons, told a nation-wide radio audience Tuesday night. Speaking as the guest of Schenley Laboratories, Inc., on the "The Doctor Fights" program dedicated to the medical profession, the distinguished Louisville surgeon cited the vast advancements in surgical technics during the present century which have resulted in far greater chances for the wounded to be restored to sound health.

HEALTH OF NEW ORLEANS

The Bureau of the Census, Department of Commerce, reported that there occurred in New Orleans the week ending July 15, 143 deaths, a very slight increase over the previous week. Of these deaths 89 occurred in the white population, 54 in the colored and 12 were in infants under one year of age. The following week, closing July 22, showed a rather small increase over the previous week; of the 155 deaths listed that week 91 were white, 64 colored and 16 were in infants. There was a sharp decrease in number of deaths occurring the week which ended July 29; 22 less deaths in the city than the previous week. Of the 133 deaths, 82 were white, 51 colored and 12 were children. For the last week of which reports are available, August 5, again there was a reduction in the number of people dying in this city. One hundred and twenty-nine citizens of New Orleans expired, 85 of whom were white, 44 non-white and 14 were infants under one year of age.

INFECTIOUS DISEASES IN LOUISIANA

For the week ending July 8 the following diseases were reported by the Louisiana State Department of Health in numbers greater than ten: Malaria 120 cases, bacillary dysentery 38, hookworm 23, mumps 22, measles 19, pulmonary tuberculosis 18, unclassified pneumonia 14, and septic sore throat 13. In addition to these more commonly reported cases there also occurred six cases of typhus fever. There were nine cases of poliomyelitis reported this week; five of which were from Orleans Parish. Most of the patients reported as having malaria were from East Carroll Parish (70) and Jackson Parish (28). The following week, which ended July 15, malaria still led other reported diseases with 73 cases, followed by 30 of pulmonary tuberculosis, 25 of mumps, 16 of typhoid fever, 14 of unclassified pneumonia and 11 of poliomyelitis. The cases of this latter disease were scattered over the state with Orleans Parish reporting four and East Baton Rouge two. The largest number of malaria cases came from East Carroll Parish, with 35. There was a considerable increase in number of cases of typhoid fever. Most of these patients were reported from parishes in the northern part of the state. For the week which concluded July 22 there were listed 82 cases of malaria, 38 of pulmonary tuberculosis, 26 of bacillary dysentery, 24 of hookworm disease, 19 of mumps, 15 each of typhoid fever, septic sore throat and unclassified pneumonia. There were five cases of poliomyelitis listed this week. The typhoid fever patients for the most part came from Caddo Parish. The following week, which terminated July 29, malaria had fallen to 29 cases but there were 22 cases of typhus fever listed and 14 of diphtheria as well as 16 cases of unclassified pneumonia. Typhus fever is almost as frequent this year as typhoid fever; of the cases reported this week, came four each from Acadia, Jefferson Davis, and Washington Parishes, three from Orleans and two from Rapides. Report for the week ending August 5, the week in which the mortality report of venereal diseases is presented, showed for this particular period 1335 cases of gonorrhea, 1136 of syphilis, 44 of chancroid and eight of lymphopathia venereum. Other common diseases included 264 cases of malaria, 125 of unclassified pneumonia, 46 of pulmonary tuberculosis, 21 of poliomyelitis, 18 of pneumococcic pneumonia and 10 of mumps. The poliomyelitis cases included 11 which should have been reported previously. No parish in the state had more than two cases except Orleans Parish, with seven cases. The total was reported by 13 parishes. From military sources came most of the cases of gonorrhea which were reported but only 193 cases of the over one thousand cases of syphilis came from this source. The malaria patients came 189 from Webster Parish and 45 from East Carroll.

DR. MARC MONROE MOUTON

1890-1944

The medical profession of Louisiana has suffered the loss of one of its most distinguished members when Dr. Mouton died the latter part of August at his home in Lafayette.

Dr. Mouton was born in 1890 and graduated from Tulane Medical School in 1913. He early settled in Lafayette where for the last few years he has been engaged in practicing his specialty of eye, ear, nose and throat. When the reform government was elected in 1939, Dr. Mouton was selected as Lt. Governor of the state. In spite of the acrimonies that arise at the time, never was a harsh word spoken about this doctor. He was quiet and gentlemanly at all times and in every respect. He was a man of strong personality yet he accomplished his aims without leaving hard feelings. As a doctor he was a real friend of man and was beloved by his very large clientele. The medical profession of Louisiana will mourn the passing of this splendid character, who always had the best interests of the medical profession near to his heart.

DR. CHARLES E. HOMAN, JR.

1898-1944

Dr. Charles E. Homan, Jr., medical director of the Ochsner Clinic, died suddenly of heart disease while in his office the evening of July 25. Dr. Homan became medical director of the Ochsner Clinic in January, 1942. He was an extremely well liked physician. Everyone who came in contact with him admired him and appreciated his always affable and pleasant manner. Like so many physicians who know that they have organic disease, he went ahead cheerfully in his chosen field and worried not about the future, which he well knew, at the best, could be only but brief.

Dr. Homan was a member of the Orleans Parish Medical Society, the Louisiana State Medical Society and the American Medical Association, as well as a member of the Amercan College of Physcans.

DR. DANTAN WYETH LANDESS

1896-1944

Dr. D. W. Landess, a graduate of the University of Tennessee in 1930 and since 1933 a member of the State Society, died suddenly of a heart attack on August 22 at the Lady of the Lake Sanitarium. He was parish health officer of West Baton Rouge, also a governor of Lions International and a high ranking officer in the Louisiana State Guard.

BOOK REVIEWS

Medcal Diagnosis: Applied Physical Diagnosis; Edited by Roscoe L. Pullen, A. B., M. D. Philadelphia, W. B. Saunders Company, 1944. Pp. 1106. 584 illus. Price, $10.00.

The reviewer approached this large volume with trepidation but quickly found that Dr. Pullen has produced a unique book of considerable merit. Thirty profusely illustrated chapters by twenty-seven authors afford authoritative descriptions of basic disorders in sufficient detail to make this an extremely useful reference work for medical students and general practitioners.

The individual contributions are inevitably not of uniform quality but no other single-volume work in English covers the specialties so thoroughly. This reviewer is incapable of commenting intelligently upon those chapters devoted to the examination of the skin, eyes, oral cavity, nose and throat, breasts and female pelvis; they seem adequate and the photographs are indeed good. Sodeman's section on the heart is outstanding in every respect and the chapter on the neurologic examination is ingeniously illustrated. Of particular utility is the section on anorectal disease and the chapters describing the study of the urologic tract, the skeletal system and the extremities provide specialty education of textbook character. Dr. Ochsner's chapter, for example, includes a description of the technic of phlebography and of procaine anesthetization of the sympathetic nervous system. There are chapters on electrocardiography and electro-encephalography, pediatric diagnosis, occupational diseases and certain general aspects of neuropsychiatry.

It is difficult to see why space was devoted to such matters as military and insurance medicine. It could have been more fruitfully occupied by a critical description of endocrine disorders. Metabolic bone disease and disorders of the neuro-muscular apparatus are neglected. There is also no chapter on blood dyscrasias although leukemia is briefly considered by the author of the section on "Examination of the Neck."

On the whole, Dr. Pullen has done an extraordinary job in assembling this book under what must have been difficult circumstances. Unfortunately, the price is too great for the average medical student.

THOMAS FINDLEY, M. D.

Safe Deliverance: By F. C. Irving, M. D. Boston, Houghton, Mifflin Co., 1942. Pp. 308. Price, $3.00.

This book is a combination of three interwoven themes; the development of obstetrics in the past hundred years, the history of the Boston Lying-In Hospital, and the highlights of the author's life. They are very skillfully treated, and the result is a most delightful volume, bubbling over with the author's humor, and filled with interesting stories of the institution and of the personalities associated with it during its hundred and ten years of existence.

The history of this hospital gives us an insight into the evolution of these institutions throughout the country in the past century. The incidental pictures of medical schools and of medical practice during this period are most informative. Unless one delves into such records, one cannot visualize the remarkable advances in medical service, due to developments in bacteriology, anesthesia, asepsis, etc., that have been made during this time. As in other fields of human endeavor, there has been more progress in the field of medicine in the past century than in all previous time covered by recorded history.

The author, being right on the scene, so to speak, gives an interesting description of the first use of anesthesia at the Massachusetts General Hospital, and of the rather disgraceful squabble between Morton and Jackson that followed. He gives proper credit to Long, of Georgia, who was really the first person to induce anesthesia with ether, but who did not establish his claim to priority by prompt publication. The development of anesthesia and analgesia in obstetrics since these early days is then described.

The author writes of the scourge of puerperal infection and its virtual elimination after the epoch making work of Pasteur and Lister. The controversy between Holmes and Meigs is described with some rather left-handed compliments for the latter gentleman. He discusses the history of cesarean section and gives some rather interesting commentary on its present-day frequency. He also touches on the evolution of the management of eclampsia, and stresses the value of the present-day policy of conservatism.

He gives quite an interesting history of the obstetrical forceps, which of course includes the story of the Chamberlen family. To quote "After a sojourn in Scotland, he (Hugh Chamberlen, Sr.) settled in 1693 in Amsterdam, where he made the acquaintance of Roger Roonshuysen, an obstetrician of that city." Let us assume that Roger was at least 25 years old by this time. Hugh is said to have sold the secret of the forceps to Roger, who, in 1747 (54 years later), managed to have a municipal law passed obliging other physicians to purchase the secret from him or from his associates. However, in 1732 (note the date) Rathlaw, another obstetrician of the city, refused to buy the secret, and persuaded Velsen, of The Hague, to help uncover the mystery. Velsen, in turn, handed the job to Van der Schwann, a student of Roonshuysen, aged, say 20. The master was foxy, and the student was persistent. He dogged Roger's steps for 61 years (so says the book), and finally

(well said, Dr. Irving), *finally*, in 1793, the "keen-eyed pupil" (now aged 81; some eyes) managed to secure the instrument and to make a sketch of it. One can only admire the ruggedness of the master and the determination of the pupil. Roger was still going strong in the practice of obstetrics at the age of 125; Van der Schwann, forsaking all ambition to establish a private practise (and probably forswearing matrimony as well), remained a pupil for 61 years, sleuthing all the while. Some men; some typesetter; some proofreader.

But to continue. The book can be heartily commended for its subject matter, its style, its humor, and the manner of presentation. It is most informative, and at the same time most delightfully written. It can be enjoyed by non-medical individuals as well as by doctors; it reads like a novel and is much more worth while.

E. L. KING, M. D.

Laboratory Methods of the United States Army: Edited by James S. Simmons, B. S., M. D., Ph. D., D. P. H. Sc. H. (Hon.) and Cleon J. Gentzkow, M. D., Ph. D., Philadelphia. Lea and Febiger, 1944. Pp. 823. Price $7.50.

This book, intended as "a manual describing practical methods for use in the medical and sanitary laboratories of the Army," has been compiled by the editors from the collaborative efforts of twenty-five contributors, many of whom are outstanding authorities in their respective fields. The result is an excellent compendium, with a wealth of useful information presented in compact yet readily accessible form. The tables summarizing data are exceedingly helpful. There are numerous maps indicating the geographic distribution of various diseases and there is an abundance of excellent illustrations, many of them colored plates.

The contents of the book include sections on clinical pathology and chemistry, mycology, bacteriology, rickettsiae and filtrable viruses; protozoology; helminthology; entomology; pathology; special veterinary laboratory methods; statistical methods. Aside from the material usually presented in such a book as this, there are numerous very useful additions, e.g. discussions of methods for liver and kidney function tests, hormonal tests for pregnancy, determination of the levels of vitamins, atabrine, quinine and penicillin in body fluids. This reviewer is particularly favorably impressed by the conciseness of the comprehensive presentations of hematology and chemistry of the blood; the rickettsiae and filtrable viruses; protozoology; and entomology.

There is often a tendency for a reviewer to be hypercritical of the work of others in the field of one's personal interest and this temptation should be resisted strongly. Nevertheless one cannot help feeling that there are several places in the discussion of bacteria of medical importance where the presentation does not seem to reflect the full appreciation of recent advances. For example, the typing of Group A streptococci by Lancefield's precipitin method is not mentioned and the preparation of extracts for grouping is not described; the serologic typing of meningococci by means of capsular swelling is deprecated; the importance of *Hemophilus influenzae* type B in meningitis and rapid diagnosis of this infection with the aid of Quellung are not considered; the practical usefulness of skin tests with bacillary antigens (as compared with cultivation of the etiologic organisms) in cases of chancroid is not discussed. It is wholely unnecessary to subculture to Endo's or eosin methylene blue agar positive cultures obtained from a patient's blood, as suggested (p. 479). It also seems a work of supererrogation to inoculate pure cultures isolated from fecal plates to both Russell's and plain agar slants, then to utilize the latter for cultural or serological identification if the reactions in Russell's double sugar medium indicate the group to which the organism belongs (p. 480). It is difficult to see why space is devoted to the genera Noguchia and Dialister in a book devoted to practical laboratory methods, since these organisms are not today regarded as of etiological significance and are unlikely to be sought for by anyone using the manual. The foregoing comments are not however to be taken as indicating that the reviewer is unfavorably impressed with the treatment of pathogenic bacteria as a whole.

There is no question but that this book will have a wide circulation and influence which it eminently merits. It will be in constant use by those interested in clinical pathology, human and veterinary infectious disease, sanitary science and others, who are fortunate enough to have a copy at hand. Its purchase is highly recommended.

MORRIS F. SHAFFER, D. Phil.

The Electrocardiogram, Its Interpretations and Clinical Applications: By Louis H. Sigler, M. D., F. A. C. P. New York, Grune & Stratton, 1943. Pp. 1074. Price, $7.50.

This volume of three hundred and ninety-one pages is divided into twenty-five chapters. In the first chapter the electrocardiogram is discussed with regard to the electrophysical, anatomical and electrophysiologic basis. There are seven diagrams in this chapter that are simple and comprehensive and should give the beginner a good knowledge of the fundamentals.

In the next chapter the recording of the heart current is described and the methods of applying the electrodes in the limb leads and the location of the precordial electrodes for the chest leads. In this chapter he makes the statement, "Although the so called fourth lead is now almost universally used, and often gives us information when the standard leads fail to do so, it does not give us all the information we desire." He thinks it is essential

that we obtain more than one precordial lead. With this the reviewer agrees for he is of the opinion that from middle life onward or in any one when coronary disease is suspected, not only all of the six precordial leads be made but one made from a point to the left of the ensiforme. This may show best the presence of a posterior inferior infarct. If the heart is greatly enlarged it may be necessary to go as far as the posterior axiliary line on a level with the apex beat.

In the chapter on The Normal Electrocardiogram it is stated, "It is true that marked abnormalities of the electrocardiogram probably rarely occur with a perfectly normal heart. Yet as our experience in electrocardiography advances, more and more electrocardiographic features previously considered as due to heart disease are found to occur in individuals who show no clinical evidence of such disease." This is in keeping with the reviewer's experience and opinion. There are reproductions of ten varieties of electrocardiograms obtained from normal adults. These reproductions are well done. They are clear cut and easy to read in detail. They include three limb leads and IV F.

In the chapter on The Electrical Axis he gives a description of the different methods used. One would gather that he thinks that the determination of the electrical axis of the QRS complex from the mere appearance of the electrocardiogram is accurate enough for ordinary use.

Under the abnormal electrocardiogram classification he emphasizes the importance of repeating the electrocardiogram at intervals and that significant changes in the curves indicate structural or functional abnormalities in the heart even if each individual tracing is of normal appearance. This is true and important and is constantly being overlooked. He divides the abnormal electrocardiogram into two parts. First the disturbance of the cardiac mechanism—second, abnormalities in the electrocardiographic patterns. He devotes one hundred thirty-five pages to the discussion of disturbances in the cardiac mechanism. This includes abnormalities due to disturbances in the sinus node; interruption of the sinus rhythm by ectopic impulses; displacement of the pacemaker; the paroxysmal tachycardias; flutter and fibrillation; the varieties of block; etc. There are many reproductions that are good with each one. There are a few words about the age, sex of the individual and clinical diagnosis with a discussion of the abnormalities seen in the electrocardiogram.

Under other abnormalities in the electrocardiogram he discusses the abnormalities of the P wave, the QRS complex, ST segment, T wave, QT interval with reproductions of curves showing these abnormalities with clinical diagnosis and with a description of the abnormalities. He stresses the importance of correlating the electrocardiogram with the clinical findings. He devotes thirteen pages to the anatomic and physiological features of the coronary circulation and its abnormalities. This chapter reflects fairly well the accepted opinions on this subject.

Coronary disease is discussed under Acute Coronary Insufficiency and Chronic Coronary Insufficiency. Under the first he includes in his discussion acute myocardial infarct; acute transit myocardial ischemia with electrocardiograms showing different types. Under chronic coronary insufficiency he places angina pectoris and mentions the varieties of the electrocardiographic changes seen in coronary sclerosis.

The subject of ventricular preponderance and of electrical axis deviation of the QRS complex is treated in two separate chapters.

Under ventricular preponderance he discusses the curves seen in right and left ventricular hypertrophy. These include the three limb leads and IV F. The chest leads from over the right and left side of the precordia might have been of additional aid.

The chapters on Myocarditis, Trauma of the Heart, Electrocardiographic Changes in Various Constitutional and Toxic States, The Effect of Drugs, and bring out the accepted views on these subjects.

The last chapter of twenty-one pages is devoted to the description of the precordial leads—CW 1 through CF 6—both normal and abnormal with a comparison of the CR & CF leads.

The bibliography at the end of each chapter falls short in some but is sufficient in most. The book is well printed and easy to read. It is stated in the preface that the book is an attempt to put the electrocardiagram in its proper perspective. One could hardly say that this has been fully accomplished. As a whole the reviewer feels that he can recommend this book to those interested in this subject.

J. M. BAMBER, M. D.

PUBLICATIONS RECEIVED

D. Appleton-Century Company, New York: Fundamentals of Internal Medicine, by Wallace M. Yater, M. D., F. A. C. P.

Lea and Febiger, Philadelphia: Surgical Disorders of the Chest, by J. K. Donaldson, M. D., F. A. C. S.

J. B. Lippincott Company, Philadelphia: The Art of Anesthesia (7th Edition), by Paluel J. Flagg, M. D.

The University of Chicago Press, Chicago: X-ray Examination of the Stomach, by Frederic E. Templeton, M. D.

The Williams & Wilkins Company, Baltimore: Clinical Urology (Second Edition), Vol. I and Vol. II, by Oswald Swinney Lowsley, A. B., M. D., F. A. C. S. and Thomas Joseph Kirwin, M. A., M. S., M. D., F. A. C. S. Manual of Urology (Third Edition), by R. M. Lecomte, M. D., F. A. C. S.